Fracture of the proximal femur in Hong Kong: dimensions, aetiology and prevention

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The research work reported in this thesis was designed and conducted by the author. Data collection for the surveys was completed with the help of Ms. R. To (research assistant). The blood assays were performed in the Department of Chemical Pathology in the Prince of Wales Hospital. The blood results were compared with normal values obtained by Dr. J. Woo in a survey of the elderly (1988). Mr. J. Chan (technician) performed the bone density measurements under the author's supervision.

Informed consent was obtained from all subjects prior to the studies. Approval had been obtained from the ethical committee of the Faculty of Medicine, the Chinese University of Hong Kong.

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Summary

Fracture of the proximal femur is an important public health problem. Little is known about the incidence and risk factors for fracture of the proximal femur in Chinese. A study on the incidence of fracture of the proximal femur; a case-control study on the risk factors for fracture of the proximal femur; a study on the vitamin D levels of patients with proximal femur fractures and a survey on the determinants of bone density in the elderly are reported in this thesis.

A survey was conducted to study the incidence of fracture of the proximal femur in Hong Kong in 1985. Data was gathered by auditing the admission records for the two main hospitals in the Kowloon region. The age, sex, area of residence and diagnosis of all patients admitted with fracture of the proximal femur in 1985 were analysed by computer. The age-specific incidence was calculated from the total number of patients living in the Kowloon region and the corresponding regional population in 1986. The result was then compared with the age-specific rates of fracture of the proximal femur in 1966 (Chalmers and Ho). The age-specific incidence rates rose in all sex and age groups. The incidence rate in women 80 years and over increased from 7 per 1000 in 1966 to 15 per 1000 in 1985.

A case-control study was conducted to investigate the risk factors for fracture of the proximal femur in Hong Kong. The risk factors studied were lack of load-bearing exercise, a low calcium intake, susceptibility to falls, smoking, alcohol consumption, medical factors and reproductive factors. A total of 400 patients and 800 controls were interviewed. Lack of load-bearing exercise was associated with an increased risk of fracture of the proximal femur. For instance, the relative risk for not walking outdoors every day was two. The calcium intake for both patients and controls were much lower than the Recommended Dietary Intake of 800 mg to 1 gm per day for Caucasians. The relative risk of proximal femur fractures increased significantly as the calcium intake decreased. Other significant risk factors included a susceptibility to falls (as indicated by a history of falls during the previous year), drinking alcohol every day, and a history of stroke.

The serum 25-hydroxyvitamin D concentration and the plasma calcium (albumin-adjusted), phosphate, and alkaline phosphatase levels were measured in 200 of the fracture patients. The results were then compared with normal values from a survey of the elderly (Woo 1988). The mean 25-hydroxyvitamin D level was lower in patients than in controls. Twenty percent of the patients had a vitamin D level which was more than 2 standard deviations below the mean of the controls, i.e. , below 14.6 μg/L for men

and 13.7 μg/L for women. Nevertheless, none of the patients with a low vitamin D level had obvious osteomalacia as indicated by their blood biochemistry.

The factors affecting bone density were studied in 80 Chinese women aged 62 to 92. Bone density at the hip and spine was measured by dual X-ray densitometry. The bone density at both the hip and spine decreased with age in this elderly population. Moreover, the bone density at the hip was positively associated with the mental test score and the body mass index. Bone density at both the hip and spine were higher in diabetic subjects, and in subjects who consumed milk regularly in the past. Bone density at neither the hip nor spine was associated with the current calcium intake, the amount of physical activity and the number of pregnancies . From multiple regression, a combination of all significant predictor variables accounted for about 30% of the variance in bone density at the hip and 20% of the variance in bone density at the spine.

Fracture of the proximal femur is a major public health problem in Hong Kong. Lack of load-bearing exercise and a low calcium intake are important risk factors. The serum 25-hydroxyvitamin D level is low in hip fracture patients, though osteomalacia is uncommon. Dual X-ray densitometry is indicated in the elderly subjects who are emaciated and demented in order to diagnose osteoporosis. Public health strategies to reduce the rising incidence of proximal femur fractures are urgently required.

Introduction

"We enter the World beneath the brim of the pelvis and exit through the neck of the femur".

Cleveland 1955

Fracture of the proximal femur is a common and significant public health and clinical problem. In 1985, about 247,000 hip fractures occurred among persons aged over 45 years in the United States (National Centre for Health Statistics 1988). The increasing incidence of the fracture in many parts of the United Kingdom has also aroused concern (Lewis et al 1981, Swanson and Murdoch 1983, Wallace 1983, Boyce and Vessey 1985). Mortality in patients with hip fractures is 10 to 20 % higher than that of normal subjects of a similar age and sex (Kreiger 1982). Many patients were unable to regain their pre-fracture level of social independence (Donaldson et al 1979), and 15 to 25 % remain in long-term care institutions for more than a year (Cummings 1985).

The incidence of fracture of the proximal femur has been low among Hong Kong Chinese in the past, and it has been postulated that hard physical labour among Chinese females may be protective (Chalmers and Ho 1970). In 1986, 7.6 % of the population in Hong Kong was aged 65 and over (Hong Kong Census and Statistics Department 1986). With urbanization, hard physical labour has become much less common in everyday life. Hence, there are reasons to contend that the problem of hip fracture may become more common locally. The results of a survey on the incidence of proximal femur fractures in Hong Kong in 1985 is reported in this thesis.

Although proximal femur fractures are associated with a high mortality, morbidity, and costs; knowledge of the risk factors is inadequate and preventive measures are controversial. Most research to date has been conducted on Caucasians 50 to 70 years old, but there is virtually no analytical study on Asians. For example, the role of dietary calcium intake and physical activity on osteoporotic fractures is unclear. Although about 90 % of fractures of the hip, forearm and pelvis result from falls (Melton III and Riggs 1983), relatively little is known about fall prevention.

A case-control study was conducted in Hong Kong on the risk factors for fractured femur. Practical hypotheses were formulated, e.g. , did frequent load-bearing exercise in the elderly reduce the likelihood of hip fracture? In addition, the vitamin D level and blood biochemistry of the patients, as well as factors affecting bone density at the hip and spine in 80 healthy elderly women were studied. The ultimate objective was to make recommendations for cheap, simple and effective measures for fracture prevention in Hong Kong's elderly population.

Fracture of the proximal femur - the dimensions of the problem

1.1 International Patterns

Melton and Riggs (1983) and Lewinnek et al (1980) calculated directly-standardized mortality rates for different countries, using the 1970 and 1977 United States populations as the standard respectively. From their calculations they discovered variations in the international patterns of fracture of the proximal femur (Tables 1(i) and 1(ii)). The standardized rates differed due to the different standard populations used, but the pattern of variation was consistent. The highest rate occurred in the USA, where Lewinnek et al (1980) reported an incident rate of 98 per 100,000 population, and Melton and Riggs (1983) reported 295 per 100,000 women in Rochester, Minnesota. The lowest rate was found in the South African Bantu and Singaporean and Hong Kong Chinese. In fact, the rate for Hong Kong in the 1970's was found to be less than one third of the rate in the USA.

Table 1(i) : Age-adjusted annual incidence of proximal femur fractures per 100,000 from various studies*

Author	Location	No. of Fractures	Incidence per 100,000 Standard Population			Femoral Neck Fractures		Average Age	
			Male	Female	Both	Male (%)	Female (%)	Male Mean (SD)	Female Mean(SD)
Affram	Malmo	1,636	32.5	105.5	69.6	60.8	77.3	72.2(13.2)	77.0(11.3)
Levine	Jerusalem	537	35.8	82.4	59.1	29.8	71.4	73.6(14.2)	75.9(11.7)
Alhava	Finland	1,442	25.6	61.5	44.0	71.6		68.7(20.4)	78.5(12.3)
Knowelden	Dundee & Oxford	530	21.4	63.2	42.8	37.1	75.7	73.3(13.1)	80.1(11.1)
Chalmers	Hong Kong	1,040	23.4	39.2	31.5	63.7		60.3(22.9)	75.4(16.5)
Wong	Singapore	642	24.0	18.9	20.3	47.5		65.1(19.2)	69.5(20.0)
Solomon	Johannesburg	78	4.9	6.2	5.6	57.0		56.0(18.9)	65.2(18.2)

* Age-adjusted to 1977 United States Caucasian population

(Source: Lewinnek GE et al. The significance and a comparative analysis of epidemiology of hip fractures. Clinical Orthopaedics and Related Research 1980;152:35-44)

Table 1(ii) : Age-adjusted incidence rates per 100,000 population for various fractures in different population groups (among person 35 years of age or older)*

Geographic locality	Proximal femur Women	Proximal femur Men	Distal forearm (or Colles) Women	Distal forearm (or Colles) Men	Proximal humerus Women	Proximal humerus Men
USA, Rochester	295.0	126.9	369.4	86.0	73.9	23.3
Sweden, Malmo	203.2	88.3	332.1	49.5	71.5	30.9
New Zealand						
Caucasians	178.3	80.9				
Maori	83.3	70.9				
Israel, Jerusalem						
American/European-born	174.6	97.2				
Native-born	145.8	92.5				
Asian/African-born	126.4	93.4				
United Kingdom, Oxford/Dundee	114.9	59.2	304.4	72.9	30.2	16.1
Finland	114.1	64.4				
South Africa, Johannesburg						
Caucasians	217.3	83.2				
Bantu	12.4	12.6				
Singapore	53.3	61.6				
Indian	268.0	117.7				
Chinese	50.3	90.9				
Malay	20.3	33.0				
Hong Kong	72.4	63.4				
Yugoslavia						
High calcium area	39.7	42.3	221.3	93.1		
Low calcium area	91.5	83.4	196.9	112.2		

* Age-adjusted to total 1970 United States Caucasians population

(Source: Melton III LJ , Riggs BL. The epidemiology of age-related fractures. In:Avioli AV ed. The Osteoporotic Syndrome. New York, Grune and Stratton 1983, p.59)

Many factors may have contributed to the variation in fracture rates. The source of data was different for each of the countries: Affram (1964) reviewed all hospital admission records in Malmo, Sweden; Alhava and Puttinen (1973) used National Board of Health Statistics in Finland; Knowelden et al (1964) used hospital records in Dundee and Oxford; and Chalmers and Ho (1970) conducted an ad hoc survey of three hospitals in Hong Kong. Although different diagnostic criteria were used in different countries, the diagnoses were based mainly on X-ray evidence. The problem of different diagnostic criteria was unlikely to be as important as in other diseases, e.g., cardiovascular disease. Lastly, the number of fracture patients not seeking hospital treatment may vary between countries. Chalmers and Ho (1970) concluded that, in Hong Kong, an injury as disabling as a hip fracture did, in fact, result mostly in a hospital admission, and the incidence rate from their survey was reliable. The observed international variation in fracture of the proximal femur was unlikely to be spurious and a genuine geographical pattern existed.

Lewinnek et al (1980) found a high correlation between fracture incidence and the latitudes of various countries. He postulated that this was due to a high prevalence of osteomalacia in the temperate countries, and osteomalacia may cause proximal femur fractures. The incidence of proximal femur fractures was associated with other factors, for example, to motor vehicles in use per capita. Lewinnek (1980) concluded that these were associations and could not be used to account for the international variation in fracture rates.

The relationship between the geographical patterns of fracture of the proximal femur and osteoporosis has also been examined in detail by Nordin (1966), who concluded that no simple pattern existed between osteoporosis and fracture of the proximal femur. The geographical patterns of fracture of the proximal femur could not be accounted for by the pattern of osteoporosis alone. For instance, in India, fracture of the proximal femur seemed more to reflect the pattern of osteomalacia than osteoporosis, and in Japan, fracture of the proximal femur was not as common as would be predicted from the prevalence of osteoporosis.

1.2 Ethnicity, sex and age

1.2.1 Ethnicity

There is a large variation in fracture rates between people of different ethnic origins (Melton and Riggs 1983) (Table 1(ii)). Negroes in America, the Maori in New Zealand and the Bantu in South Africa all had lower fracture rates than Caucasians living in the same country. In Singapore, the rate was highest among Indians and lowest among Malays.

In some studies, environmental factors were controlled. Bollet et al (1965) found that the age-adjusted rate for Caucasians was about twice as high as that of Negroes in Charlottesville, Virginia. Engh et al (1968) studied institutionalized Negro and Caucasian populations and found that the fracture rate was 4-6 times higher in Caucasians than in Negroes. These studies highlighted the ethnic variations in fracture of the proximal femur.

1.2.2 Sex

The female-to-male ratios of incidence rates for fracture of the proximal femur have been calculated by Lewinnek et al (1980) and is presented in Table 1(iii). The ratio varied from 0.58 in Singapore to 2.75 in Sweden,i.e. ,highest in the high incidence countries and lowest in the low incidence countries.

The female-to-male ratio was 1.15 in Hong Kong and 0.58 in Singapore. One possible explanation for these observations is that Chinese females might be less likely to present themselves to 'western' practitioners and hospitals. However the results of a survey by Chalmers and Ho (1970) showed that, for such a debilitating condition as a fractured femur, most patients availed themselves of hospital treatment. Hence, the observed low sex ratios in Hong Kong and Singapore were unlikely to be due to cultural differences in consultation patterns alone.

The reasons for the relatively low incidence of fracture of the proximal femur for Chinese women in Hong Kong and Singapore have been widely discussed. Chalmers and Ho (1970) and Wong (1967) postulated that heavy physical labour protected Chinese women against osteoporosis and fractured femur, but this has not been proven by intrapopulation studies.

Table 1(iii): Female to male ratios for fracture of the proximal femur

	Rates per 100,000* Women	Men	Female/Male Ratios
United States (Rochester)	101.6	50.5	2.01
New Zealand	96.8	35.2	1.79
Sweden	87.2	38.2	2.75
Jerusalem	69.9	42.8	1.63
United Kingdom	63.1	29.3	2.15
Holland	51.1	28.5	1.80
Finland	49.9	27.4	1.78
Yugoslavia (low calcium area)	39.2	37.9	1.03
Yugoslavia (high calcium area)	17.3	18.2	0.95
Hong Kong	31.3	27.2	1.15
Singapore	15.3	26.5	0.58
South African Bantu	5.3	5.6	0.94

* standardized to 1970 United States Caucasians population.

(Source: Gallagher JC. Epidemiology of fractures of the proximal femur in Rochester, Minnesota. Clinical Orthopaedics and Related Research 1980; 150:163-171).

1.2.3 Age

The variation in incidence of fractured femur with age is consistent between countries (Stewart 1955, Buhr and Cook 1959, Affram 1964, Knowelden 1964, Alhava and Puttinen 1973, Gallagher et al 1980(b), Chalmers and Ho 1970, Boyce and Vessey 1985). Proximal femur fractures are rare in populations younger that 50 years and increase exponentially with age thereafter. A similar pattern was observed in Chinese (Chalmers and Ho 1970).

Nordin (1968) found that a reduction in spinal density and metacarpal cortical thickness first becomes apparent in women in the 5th and 6th decades and the fall in bone density continues with aging. A similar but less pronounced trend occurs in men. Hence the age and sex patterns of fractured femur simulate the pattern of osteoporosis, and this suggests that the variation of the fracture with sex and age reflects the loss of trabecular bone with ageing, especially in women.

Table 1(iv): Age-specific rates of proximal femurs fractures (1965-1974, Rochester, U.S.A.)

	Age (Years)	Men Cases	Men Rate*	Women Cases	Women Rate*	Combined Sexes Cases	Combined Sexes Rate*
Cervical fractures							
	< 50	4	2.1	3	1.4	7	1.7
	50-59	31	6.0	9	37.2	12	27.9
	60-69	4	30.8	32	160.2	36	109.1
	70-79	8	102.6	50	340.1	58	257.7
	80+	18	562.5	68	895.9	86	797.0
Trochanteric fractures							
	< 50	8	4.2	1	0.5	9	2.2
	50-59	4	21.4	6	24.8	10	23.3
	60-69	8	61.5	18	90.0	26	78.8
	70-79	7	89.7	49	333.3	56	248.9
	80+	23	713.8	92	1212.1	115	1065.8

* Number of cases per 100,000 population per year.

(Source: Gallagher JC. Epidemiology of fractures of the proximal femur in Rochester, Minnesota. Clinical Orthopaedics and Related Research 1980;150:163-171).

1.3 Secular trends

In recent years the increasing incidence of fracture of the proximal femur in England and Wales has aroused concern. Wallace (1983) documented a two-fold increase in incidence in Nottingham and described this as an 'orthopaedic epidemic'. Boyce and Vessey (1985) found a similar two-fold rise in incidence in Oxford. Both authors emphasized the necessity to investigate the aetiology of the fracture. The increase in fracture rates has been similarly documented by Swanson and Murdoch (1983) in Dundee and by Lewis (1981) for the whole of England and Wales. Zetterberg and Anderson (1982) found a statistically significant age-specific increase in fracture incidence from 1940 to 1979 in Gotterberg. Their findings were not supported by Nilsson and Obrant(1978), who showed that the rate had ceased to increase after 1968.

However, an increase in incidence has not been demonstrated in the USA. Melton et al (1982) studied the incidence of hip fractures from 1928 to 1977 in Rochester, Minnesota. Although the rates increased during the first 15 years of the study, the age-adjusted incidence for both sexes remiained unchanged thereafter.

Little is known about the change in incidence in Asian countries where the rate has been low in the past. In Chapter two of this thesis, the results of a recent survey in Hong Kong is presented and comparisons will be made with other countries.

Survey of fracture of the proximal in Hong Kong

2.1 Sources of health statistics in Hong Kong

The medical and health services in Hong Kong are organized on a regional basis. Hospital and clinic facilities situated in a common geographical area form an integrated network of services. In 1985-86 there were three types of hospitals in Hong Kong - government, subvented and private - with a total of 24638 beds representing 4.5 beds per 1000 of the population (Director of Medical and Health Services 1986).

The only source of health statistics published in Hong Kong are in the annual report of the Director of Medical and Health Services. Unlike Britain, where information can be readily obtained from the Hospital In-Patient Enquiry and the Hospital Activities Analysis, ad hoc surveys have to be carried out when information on dimensions of health problems is being sought.

2.2 Objectives of the survey of fracture of the proximal femur in Hong Kong

Since Chalmers and Ho (1970) first documented 20 years ago that the rate for fracture of the proximal femur was low in Hong Kong Chinese, the secular trend of the fracture has not been studied. The main objective of the survey reported here was to estimate the age and sex specific fracture rates in 1985. It was also designed to describe the seasonal variations in fracture rates and the average duration of hospital stay.

2.3 Methods

2.3.1 Survey methods

The survey was conducted in the Kowloon region. This is the most densely populated area in Hong Kong, with about 800,000 people living in an area of 12 square Kilometres. This region is served by two hospitals: Queen Elizabeth Hospital, a government hospital and Kwong Wah Hospital, a subvented hospital.

The hospital admission records for the Orthopaedic Units of both hospitals for 1985 were audited. For each patient admitted with fracture of the proximal femur, the following data were gathered: sex, age, diagnosis on admission, area of residence, dates of admission and discharge. The data was processed by the statistical package Data-Base III on a microcomputer.

It was found that a large proportion of patients did not live in the region served by these regional hospitals. The location of each patient's home was scrutinized, and only those patients living in the Kowloon region (Kowloon City, Mongkok, Yau Ma Tei) admitted for hip fracture was included in the calculation of incidence rates. The regional population for 1986 from the census was used for calculation of age-specific rates.

2.3.2 The methods of calculating standardized fracture rates

Lewinnek (1980) calculated directly standardized hip fracture rates for various countries using the 1977 USA population as the standard. In order to adjust for difference in population structure and to obtain comparable incidence rates, the 1985 hip fracture rates for Hong Kong were similarly standardized to the 1977 USA Caucasian population.

The method of direct standardization was used. The age-specific fracture rates for each 10-year age group was applied to the standard population,i.e.,the USA 1977 Caucasian population. The total number of fractures expected in the standard population can then be calculated, and this number divided by the total standard population for each sex resulted in the directly standardized hip fracture rates(table 2 iii).

2.4 Results and discussions

2.4.1 Age - and sex-specific rates

Table 2(i) and Fig 2(i) show the age and sex distribution of all fracture of the proximal femur patients admitted in 1985. A total of 878 patients were admitted to the two hospitals for fracture of the proximal femur in 1985. Only 389 of these patients lived in the Kowloon region (Kowloon City, Mongkok, Yau Ma Tei) and they formed the numerators for calculating age- and sex-specific rates.

Table 2(i). Age and sex distribution of the fracture of the proximal femur patients admitted in 1985

Age group	Males	Females
< 40	37	21
40-49	15	6
50-59	23	25
60-69	41	96
70-79	92	208
80-89	51	192
>=90	11	57
Total	275	605

Figure 2(i): Age and sex distribution of the fracture of the proximal femur patients admitted in 1985

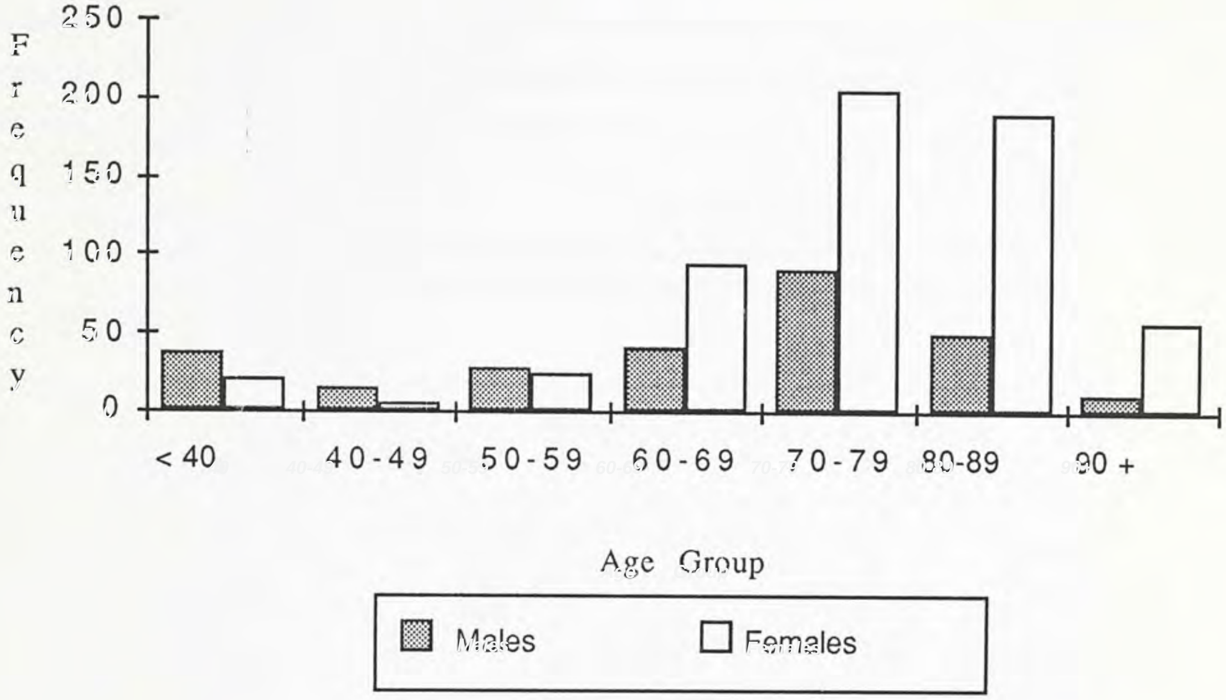


Table 2(ii) shows the number of patients and the total population for the Kowloon region (Kowloon City, Mongkok, Yau Ma Tei). These were used in calculating the sex-specific rates.

Table 2(ii): Data for calculation of age- and sex-specific rates for fracture of the proximal femur in Kowloon region (Kowloon City, Mongkok, Yau Ma Tei) in 1985

	Male		Female	
Age group	No. of patients	Population	No. of patients	Population
< 40	11	262,626	7	239,099
40-49	6	44,751	4	36,547
50-59	13	47,103	12	37,660
60-69	16	29,400	41	30,394
70-79	44	12,999	94	18,766
80 +	31	2,681	110	7,232

Table 2 (iii) and Fig 2 (ii) show the age- and sex-specific rates for fracture of the proximal femur in the Kowloon region. There was a noticeable increase in fracture rates among the elderly (in males 70 years or older and in females 60 years or older). Chalmers (1970) suggested that the relatively low fracture rates among Chinese women could be attributed to heavy physical labour. The rate of industrialization and urbanization has been dramatic in recent decades in Hong Kong, as a result heavy physical labour has become less necessary. This may account for the increase in fracture rates over recent years. The incidence of fracture of the proximal femur was higher in females than in males for all age groups. In 1985, there was an acute increase in incidence after the age of 70 years and again after the age of 80 years for both men and women.

Table 2(iii): Age-specific rates (per 100,000 population) for fractured proximal femur in 1966 (for the whole of Hong Kong) and 1985 (for the Kowloon area)

Age group	Males 1966*	Males 1985	Females 1966*	Females 1985
< 40	1.0	4.1	0.2	2.9
40-49	6.1	13.4	6.9	11.0
50-59	16.5	27.7	22.6	31.9
60-69	71.2	54.4	57.3	134.9
70-79	224.4	338.5	172.5	500.9
>=80	320.5	1156.3	716.3	1,521.2

(* calculated from data published by Chalmers and Ho, 1970)

Figure 2(ii): Age-specific rates (per 100,000 population) for fracture of the proximal femur in 1966 (for the whole of Hong Kong) and 1985 (for the Kowloon region)

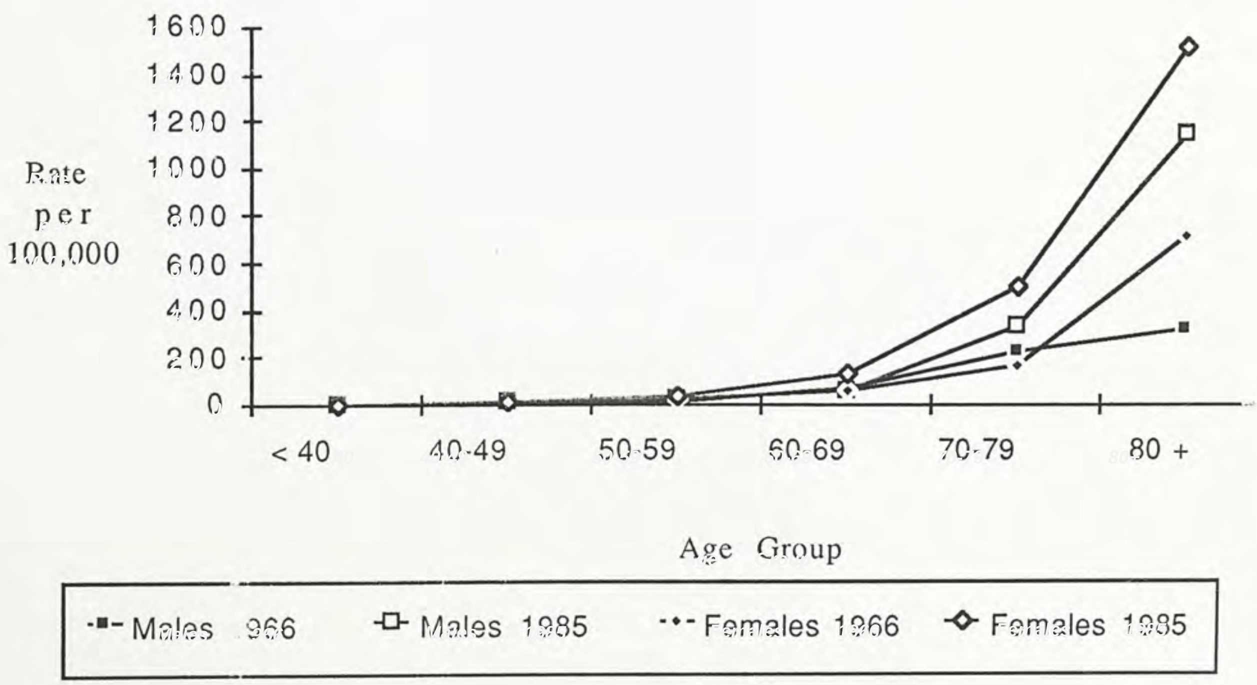


Table 2(iv) shows the directly-standardized rates for fracture of the proximal femur using the 1977 USA Caucasian population as the standard (source: Lewinnek et al, 1980). The rate increased among men increased from 23.2 per 100,000 in 1970 to 42.1 per 100,000 in 1985 and from 39.2 per 100,000 in 1970 to 87.3 per 100,000 in 1985 among women.

Table 2 (iv): Directly standardized rates for fracture of the proximal femur in Hong Kong (using the 1977 USA Caucasian population as the standard)

Age (years)	Standard Population with age and sex distribution of US 1977 Male (a)	Female (b)	Hip fracture rates per 100,000 (Hong Kong 1985) Male (c)	Female (d)	Expected no. of fracture Male (a x c)	Female (c x d)
< 40	32,179	31,673	4.1	2.9	1.32	0.92
40-49	5,171	5,434	13.4	11.0	0.69	0.60
50-59	5,063	5,505	27.7	31.9	1.40	1.76
60-69	3,726	4,451	54.4	34.9	2.03	6.00
70-79	1,901	2,730	338.5	500.9	6.43	13.67
>=80	748	1,432	1,156.3	1,521.2	8.65	21.7
Total	48,788	51,225			20.52	44.73

	Male	Female	
Directly Standardized Rate	20.52/48788 = 42.06	44.73/51225 = 87.32	per 100,000

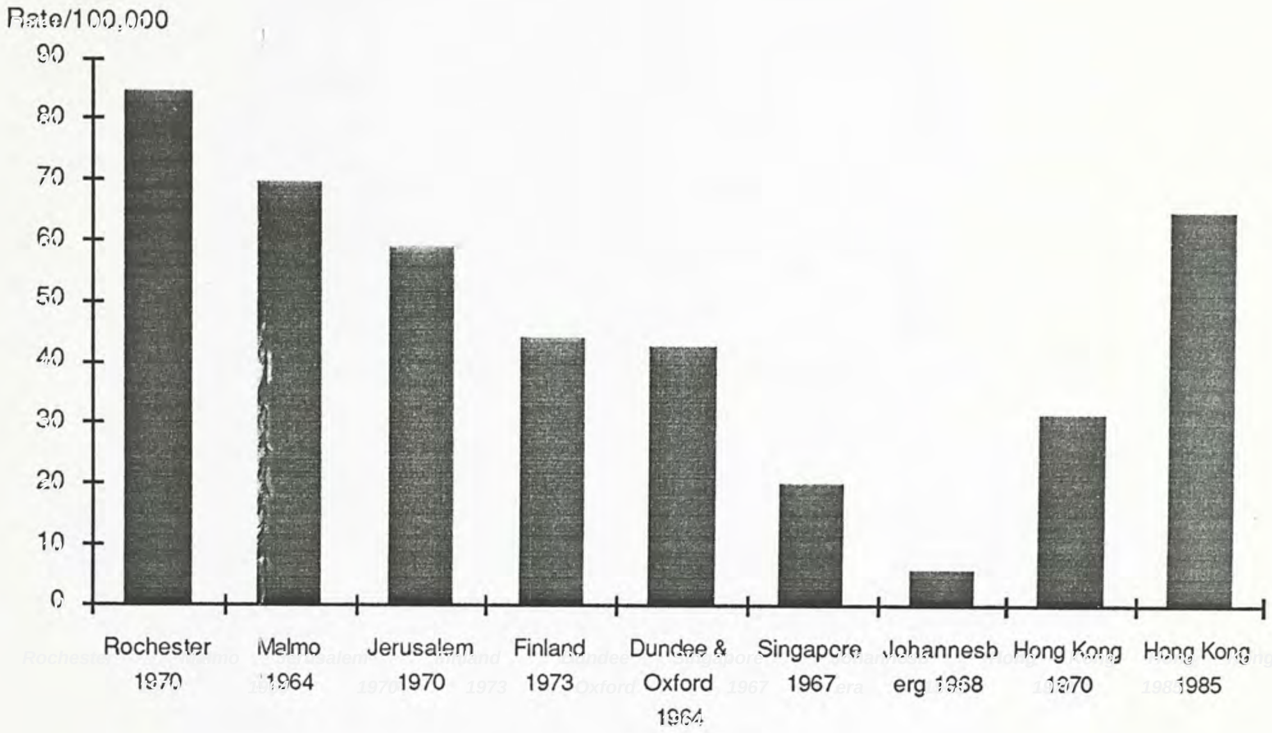
The standardized rates in Hong Kong were compared with similarly standardized rates from other countries in Table 2(v). The directly standardized rates in both men and women were higher than similarly standardized rates in Jerusalem (Levines 1970), Finland (Alhava 1973) and England (Knowelden 1964). Among men, the rate was as high as the rate in the USA, although the rate among women in Hong Kong was not as high as that in the USA.

Table 2 (v): Age-adjusted annual incidence of hip fractures per 100,000 population from various studies (standardized to 1977 United States Caucasian population)

Author	City/Country	Year	Incidence per 100,000 standard population		
			Male	Female	Both
Gallaghar	Rochester	1970	42.8	111.5	84.7
*Affram	Malmo	1964	32.5	105.5	69.6
*Levine	Jerusalem	1970	35.8	82.4	59.1
*Alhava	Finland	1973	25.6	61.5	44.0
*Knowelden	Dundee & Oxford	1964	21.4	63.2	42.8
*Wong	Singapore	1967	24.0	18.9	20.3
*Solomon	Johannesburg	1968	4.9	6.2	5.6
Chalmers	Hong Kong	1970	23.4	39.2	31.5
Lau	**Hong Kong**	**1985**	**42.1**	**87.3**	**65.3**

(* Source: Lewinnek GE et al. The significance and a comparative analysis of epidemiology of hip fractures. Clinical Orthopaedics and Related Research 1980;152:35-44)

Fig 2 (iii): Age-adjusted annual incidence of hip fractures per 100,000 population from various studies (standardized to 1977 United States Caucasian population)



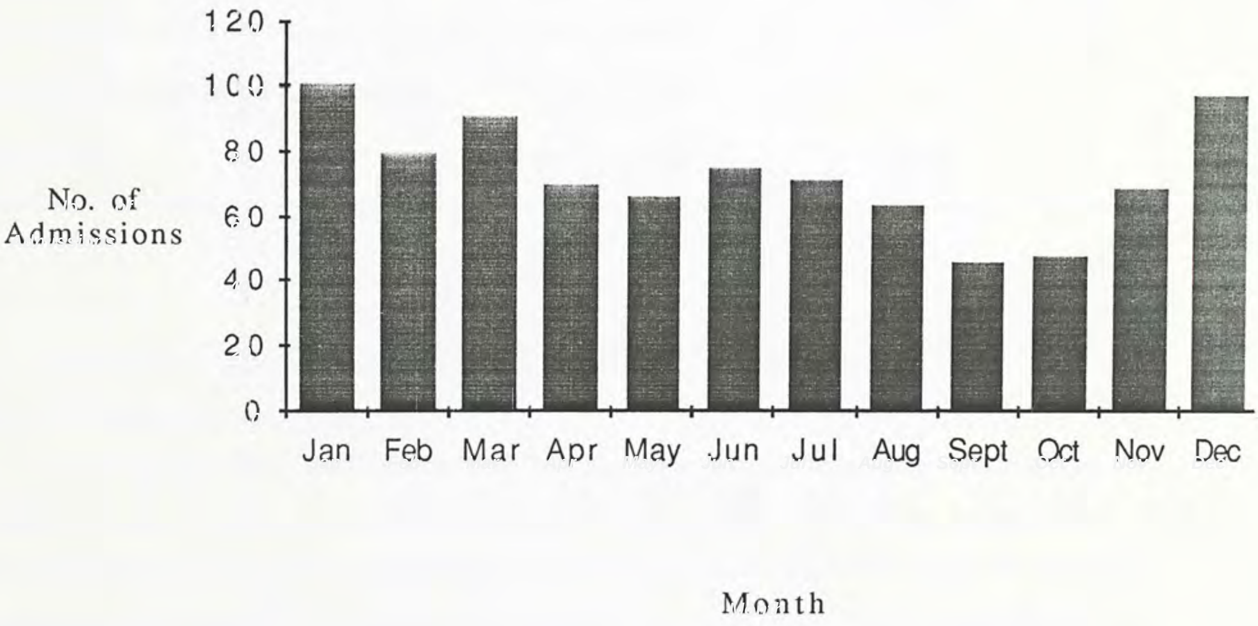
2.4.2 Seasonal variations in the incidence

The total number of proximal femur fracture patients admitted to the two surveyed hospitals is presented by months in Table 2(vi) and Figure 2(iii). The peak rates occurred during the winter months (December and January), while the rates were lowest in the summer months (May to September). Zetterberg (1982) documented a moderate increase in fracture incidence in winter in Sweden. Melton (1983) described a seasonal pattern of proximal femur fractures in Rochester, Minnesota, although the variation was much less substantial than for forearm fractures.

Table 2(vi): No. of admissions for fracture of the proximal femur by months

Month	No. of Admission
January	101
February	80
March	91
April	70
May	66
June	75
July	72
August	64
September	46
October	48
November	69
December	98

Figure 2(iv): No. of admissions for fracture of the proximal femur by months



Hong Kong winters are relatively mild with a mean monthly temperature about 17 degrees C. Nevertheless, heating systems are absent in most homes, so the elderly dress heavily in winter. Most elderly Chinese believe that it is unhealthy to be exposed to the cold wind outdoors, and as a result most old people are physically much less active in winter. Dressing heavily and a lack of activity can contribute to poor coordination and being prone to falls, which may explain the increase in fracture rates. Alternatively, a decreased exposure to sunlight may be associated with an increased fracture tendency in winter.

2.4.3 Duration of hospital stay

The duration of hospital stay for fracture of the proximal femur patients is presented in Table 2(vii). Ninety-five percent of all patients who survived post operatively in Queen Elizabeth Hospital were transferred to Kowloon Hospital for rehabilitation, and this substantially shortened the mean stay in Queen Elizabeth Hospital. The range and mean days of stay were similar in men and women in both hospitals. The maximum length of hospitalization was 3 months.

Table 2(vii): Length of hospital stay for all fracture of the proximal femur patients in two hospitals

	Kwong Wah Hospital		Queen Elizabeth Hospital	
	Male	Female	Male	Female
Mean length of hospital stay (days)	25	27	12	12
Range (days)	1-96	1-90	1-80	1-91

2.5 Postulated factors for the increasing incidence of the fracture

2.5.1 Possible sources of error

The age-specific incidence rate of hip fracture was calculated by the number of patients living in the region and the regional population. There was no problem of overestimation as all patients who were from other regions were excluded. To estimate the proportion of patients who were from the Kowloon region but who were admitted to other hospitals, a survey was subsequently conducted in Caritas Medical Centre. This hospital is located in Shamsuipo in New Kowloon, and serves part of New Kowloon. A total of 108 women and 62 men were admitted for hip fractures in 1985. Of these, only eight women and five men were from the Kowloon region. As the total number of patients for calculating the age-specific rates for the Kowloon region was 389, this seemed to indicate that a relatively small proportion of patients had been admitted to other hospitals,e.g., Caritas Medical Centre. The age-specific rates may have been only slightly underestimated. This implies that the age-specific rates for 1985 might be slightly higher than what is presented, but there was no overestimation, as explained earlier.

Chalmers and Ho calculated the incidence of hip fracture in 1970 using admission data from the three main regional hospitals in Hong Kong at that time. In order to ascertain that most patients with hip fracture were admitted, they conducted a survey of bone-setters. They concluded that most patients with hip fracture were admitted to hospital, and the incidence rates were reliable.

Hence it may be concluded that there was a genuine increase in the incidence of hip fracture in Hong Kong from 1970 to 1985, and the possible reasons for this observation are discussed below.

2.5.2 Change in population structure

The proportion of the elderly in the population increased steadily from 1961 to 1986 (Table 2 viii). Age-specific rates were calculated here to adjust for the increase in the rate of fracture concomitant with the increase in the proportion of elderly people in the population. Part of the increase in fracture rates in the population 80 years old and over may be attributed to an increase in the very old population,i.e., 90 and above. Nevertheless the effect is probably too small to account for the three-fold increase in age specific rate in the age group 80 years or above.

Table 2(viii): Percentage of the elderly (65 years and over) in the population from 1961 to 1986

Year	Percentage
1961	2.8
1966	3.3
1971	4.5
1976	5.5
1981	6.6
1986	7.6

(Source: Hong Kong Census and Statistics Department 1978, 1981)

2.5.3 Urbanization

The influx of people from Mainland China between 1949-51 suddenly swelled the urban population in Hong Kong and created huge employment and social welfare problems. In the mid-1960's, there was a boom in local industrialization and further urbanization

(Sit 1981). To illustrate the pace of urbanization, the percentage of built-up land in Hong Kong is presented in Table 2(ix).

With urbanization, many districts in Hong Kong have been rebuilt. There is a notable deficiency in open space in almost all residential areas; and the usage of land has been extremely varied, e.g., industrial factories cheek by jowl with residential units. Since the beginning of urbanization, many families have been cramped into single-space cubicles (Pryor 1981).

Table 2(ix): Percentage of built-up land in Hong Kong

Year	Percentage
1966	9.6
1971	11.3
1976	12.4
1981	16.0

(Source:Hong Kong Census and Statistics Department 1983)

2.5.4 Lack of physical activity

With urbanization, the proportion of the population engaged in heavy manual labour has decreased. The percentage of farmers and fishermen dropped from 8% in 1961 (Hong Kong Census and Statistics Department 1969) to 2% in 1981 (Hong Kong Census and Statistics Department 1983).

As a consequence of the lack of open space, the opportunity for physical recreational activity was also reduced. The Biosocial Survey conducted in Hong Kong showed that only 8% of subjects 50 to 59 years old reported that they had visited the beach recently, and 90% said that they never engaged in physical recreational activity (Millar 1979).

2.5.5 Environmental factors

With the construction of massive high-rise buildings and a sudden change in the environment, the pattern of accidents and falls among the elderly has also changed. An increased susceptibility to falls is also a potential factor in the increasing incidence of fracture of the proximal femur.

Controversies in risk factors for fracture of the proximal femur

3.1 Introduction

Fracture of the proximal femur arises from many medical, social and behavioral factors. Although osteoporosis is the main predisposing cause, other factors may be implicated. These include a tendency to falls in the elderly (Aitken 1984 a), and diminished ability to counteract the fall (Melton and Riggs 1985). The relative importance of the risk factors for osteoporosis are unclear, and no epidemiological studies have been conducted in Chinese to investigate these.

3.2 Osteoporosis and fracture of the proximal femur

Although osteoporosis is widely accepted as the most important determinant of hip fracture incidence (Consensus Development Conference 1987), it may not be the sole cause of the fracture (Evans et al 1981, Wicks et al 1982, Aitken 1984a, Cummings 1985).

The numerous studies conducted to investigate whether patients with fracture of the proximal femur are more osteoporotic than the 'normal' population are summarized in Table 3(i). The different results may be due to differences in methodology.

Table 3(i): Summary of studies conducted on osteoporosis and fracture of the proximal femur

a) Studies in which a positive association between osteoporosis and fracture of the proximal femur was demonstrated

Author	Year	Study Population	Epidemiological Method	Methods for measuring bone density
Stevens et al	1962	Glasgow, UK	Case-control	histomorphometry of iliac crest, radio-grammetry at 3 sites
Iskrant & Smith	1969	Michigan, USA	Cohort	radiography of spines
Aaron	1974	Leeds, UK	Case-control	histomorphometry of iliac crest
Pogrund et al	1977	Jerusalem	Case-control	radiography of spines
Matkovic et al	1979	Yugoslavia	Cohort	X-ray morphormetry of hands
Horsman et al	1982	Leeds, UK	Case-control	Radiography of hands and hips
Melton et al	1986	Rochester, USA	Cohort	Dual photon absorptiometry of proximal femur

Table 3(i): Summary of studies conducted on osteoporosis and fracture of the proximal femur

b) Studies in which no association between osteoporosis and fractured proximal femur was demonstrated

Author	Year	Study Population	Epidemiological Method	Methods to measure bone density
Faccini et al	1976	London, UK	Case-control	histomorphometry of iliac crest
Wootton	1979	London, UK	Case-control	photon-absorptiometry forearm
Elasser et al	1980	Middlesex, UK	Case-control	computerized tomography of distal radius
Evans et al	1981	Australia	Case-control	X-ray morphometry of hands histomorphometry iliac crest
Riggs	1982	Rochester, USA	Case-control	photon-absorptiometry of femoral neck and intertrochanteric region
Krolner & Nielsen	1982	Denmark	Case-control	Dual-photon absorptiometry of spine
Wicks et al	1982	Adelaide, South Australia	Case-control	histomorphometry of femur
Bohr & Schaadt	1983	Urban Copenhagen	Case-control	dual photon absorptiometry of femur
Aitken	1984	Colchester, UK	Case-control	x-ray morphometry of hands

3.2.1 Populations studied

The studies were conducted in Copenhagen and Jerusalem, as well as various parts of the UK, the USA, and Yugoslavia, . The extent of osteoporosis may vary in hip fracture patients of different ethnicity, and generalization is difficult. None of these studies was conducted for an Asian population.

3.2.2 Selection of cases and controls

With the exception of 3 cohort studies (Iskrant and Smith 1969, Matkovic et al 1979, Melton et al 1986), the bone density of 'cases' and 'controls' were compared. Methodological problems existed for some of these case-control studies.

The selection of cases and controls was a potential source of bias. Ideally, the cases should comprised a complete sample of fracture patients within a defined population , and the controls should be a random sample of the population without the disease (Schlesselman 1982). In some of these studies, the cases or subjects were highly selected. For example, Bohr and Schaadt(1983) excluded very sick and hemiplegic patients, Krohner and Nielsen (1982) used referred cases, and Riggs (1982) investigated only ambulatory survivors at one year after the fracture. Although all these authors demonstrated that osteoporosis was not an important risk factor for fracture of the proximal femur, this finding could have resulted from the selection bias towards patients who were not osteoporotic. Similarly, controls selection could introduce bias in the results. Two of the case-control studies (Elasser et al 1980, Evans et al 1981) used orthopaedic patients as controls. The bone density of patients with orthopaedic problems can hardly be assumed to be representative of a normal population, e.g., patients with osteoarthritis may be more heavily built than in general. The use of autopsy controls (Faccini et al 1976, Wicks et al 1982) and volunteers (Riggs 1982) might also have introduced selection bias.

3.2.3 Measurements of bone density

It can be seen from Table 3(i) that not all authors measured bone mass at the hips. Measurements of cortical bone at sites other than the proximal femur and iliac crest are of doubtful validity because the degree of osteoporosis may vary between different sites on the skeleton.

Three methods have been used to measure bone density at the hip: iliac crest histomorphometry (Stevens et al 1962, Aaron 1974, Faccini et al 1976, Evans et al 1981), radiogrammetry of the proximal femur (Horsman 1982) and photon absorptiometry of the femoral neck (Riggs 1982, Bohr and Schaadt 1983, Melton et al 1986).

Histomorphometry measures trabecular bone density directly but bone biopsies are of greater value for measuring bone turnover (Aitken 1984 b). Some authors have found the Singh Index to be of variable reliability (Cooper et al 1986). The high validity of photon absorptiometry in measuring bone mass is best proven (Wahner et al 1977, Smith et al 1974, Mazess et al 1973). Different methods of measuring bone density may produce different results.

Recently Melton et al (1986) conducted a cohort study by measuring trabecular bone mass in the proximal femur . The absolute and relative importance of osteoporosis in fracture of the proximal femur were studied. The risk of proximal femur fracture was found to be highly associated with bone density at the site of fracture. However, he concluded that osteoporosis was not the sole cause of fracture, and other independent risk factors for fractured femurs may exist. This was supported by earlier works from other authors (Rodstein 1964, Ashley et al 1977).

3.3 Risk factors for osteoporosis

Osteoporosis can be defined as a reduction in bone density (Nordin 1983) i.e. when the bone mass per unit volume falls below the lower normal limit. Albright (1947) originally hypothesized that osteoporosis exists in two forms: postmenopausal osteoporosis and senile osteoporosis. This concept has been modified by Riggs and Melton (1983), who proposed that primary osteoporosis can be classified into two types.

Type I (postmenopausal) osteoporosis is presumably caused by oestrogen deficiency which occurs in postmenopausal women . This primarily affects trabecular bone, and results in fracture of the spine and forearm. Type II (senile) osteoporosis occurs in the elderly. This results from impaired bone formation and increased bone resorption associated with impaired calcium absorption. It affects both cortical and trabecular bone and leads to fractures of the hip and forearm.

The risk factors for osteoporosis include oestrogen deficiency, physical inactivity, calcium deficiency, smoking, alcoholism, certain diseases and drug treatments. None of these factors per se can account for the geographical pattern of osteoporosis nor the increasing incidence of fracture of the proximal femur in some countries. The roles of these factors are discussed below.

3.3.1 Oestrogen deficiency

3.3.1.1 Menopause and other reproductive factors

Post-menopausal osteoporosis was first introduced as a clinical entity by Albright et al (1941). Vertebral fractures occur six times more frequently in elderly women than in men (Meema et al 1965), implying that oestrogen deficiency is important in the aetiology of osteoporosis. Both cortical and trabecular bone show an accelerated loss in the early postmenopausal period (Davis et al 1966, Mazess et al 1982). Nevertheless, this loss began before menopause, and occurred also in men (Mazess et al 1982).

The age at menarche, at first pregnancy, menopausal symptoms and variations of the menstrual cycle do not appear to be related to the risk of fracture of the proximal femur (Kreiger 1982). Contrary to earlier reports, recent evidence has suggested that multiparity and prolonged breast feeding protected women against osteoporosis and hip fractures (Smith 1967, Daniell 1976, Wyshak 1981, Aloia et al 1983). The use of oral contraceptives has been associated with somewhat greater cortical bone mass (Goldsmith and Johnston 1975, Kanders et al 1984). Osteoporosis has been reported to be a complication of anorexia nervosa (Rigotti et al 1984).

3.3.1.2 Oophorectomy and osteoporosis

Meema et al (1965) investigated the effects of oophorectomy on bone density retrospectively. The study was conducted on oophorectomized patients including those with cancer. Nordin (1968) conducted a similar study by measuring bone density at the spine. The results of both studies showed that bone density was significantly lower in oophorectomized women than women with intact ovarian function.

More recently, Richelson et al (1984) compared 14 women who had undergone oophorectomy during young adulthood with perimenopausal and postmenopausal women. The pattern of bone loss in the oophorectomized group resembled that in the postmenopausal group.

3.3.1.3 Oestrogen therapy and osteoporosis

Results from case-control studies demonstrated that oestrogen replacement is a protective factor for osteoporosis (Hutchison et al 1979, Weiss et al 1980, Paganini-Hill et al 1981, Kreiger 1982). Recent findings from the Framingham study showed that the adjusted relative risk for hip fractures in women who had taken estrogen within the previous two years was 0.34 (Kiel et al 1987). Both case-control studies designed to determine the effect of dosage (Paganini-Hill et al 1981, Weiss et al 1980) showed negative results.

The evidence from follow-up studies and clinical trials supported the findings from the case-control studies (Table 3(ii)). Although these trials differed in design and different dosages of oestrogen were used, the beneficial effects of oestrogen administration in preventing osteoporosis was obvious. The minimum effective dose seemed to be 0.625 mg of conjugated oestrogen (Table 3 (ii). The effectiveness of estrogen therapy started several years after the menopause and the duration of protection after the cessation of therapy is questionable (Ernster et al 1988).

Table 3(ii): Follow-up trials on oestrogen replacement therapy and fracture of the proximal femur in postmenopausal women

Author/Year	Sample size	Treatment	Method of measuring bone density
Davis et al,1966	87	0.5mg Diethyl stilbestrol	absorptiometry of hand
Riggs,1972	17	0.5mg conjugated oestrogen	bone histomorphometry
Gordon et al ,1973	220	1.25 mg conjugated oestrogen	no. of vertebral fractures
Aitken ,1973	147	20µg mestranol	x-ray densitometry of hand
Lindsay , 1976	120	24.8µg mestranol	photon absorptiometry
Nachtigall et al ,1979	84	2.5mg conjugated oestrogen	photon absorptiometry of hand
Ettinger et al ,1985	18	0.9mg equine oestrogen	CAT scanning of vertebrae

3.3.2 Calcium intake

3.3.2.1 Calcium requirements

Based on metabolic balance studies, Nordin et al (1979) estimated that a calcium intake of 550 mg per day was required to prevent a negative calcium balance. Heany et al (1982) estimated the calcium requirement to be 1000 mg per day for premenopausal and 1500 mg per day for postmenopausal women. Some authors (Hegsted 1963, Walker 1972) disagreed that there is a definite calcium requirement in human subjects.

3.3.2.2 Calcium intake, bone mass and osteoporosis

The variation in dietary calcium intake cannot account for the geographical pattern of osteoporosis. In general, populations with a low dietary calcium, protein, and vitamin D intake have a low incidence of osteoporotic related fractures (Melton III and Riggs 1983). Nevertheless, the effects of a low dietary calcium intake might have been offset in these populations by a low protein and salt consumption, or by a high level of physical activity. In Yugoslavia, the incidence of proximal femur fractures was higher in an area with low calcium intake than an area with high calcium intake (Matkovic et al 1979).

Many cross-sectional studies have been conducted to investigate the relationship between dietary calcium intake and absolute bone mass. In these studies, calcium intake has been assessed by different methods, and bone mass has been measured at different sites. Smith (1965) and Garn (1970) both failed to showed any positive association between calcium intake and bone density. Hurxthal (1969) and Garn (1981) obtained positive results but these were not statistically significant.

Nordin et al (1979) and Riggs et al (1967) compared the dietary calcium intake of osteoporotic patients and controls by a case-control method. They both demonstrated that the calcium intake of osteoporotic patients was lower than that of controls. The findings by Hurxthal and Vose's (1969) were similar but the differences were not statistically significant. Although these studies differed in methods and rigor, in general osteoporotic subjects seemed to consume less calcium than controls. Moreover, osteoporosis has been found to be more common among patients with lactase deficiency (Birge et al 1967, Newcomer et al 1968, Finkenstedt et al 1986).

3.3.2.3 Calcium therapy and osteoporosis

Many clinical trials have been conducted to test the effects of calcium supplementation on bone density. In these studies, the effects of calcium supplemention of about one gram per day were tested. A recent study by Riis et al (1987) showed that calcium supplement retarded the rate of loss of cortical bone, but had no effect on trabecular bone. Lamke et al (1978) and Nilas et al (1984) also demonstrated that the rates of bone loss at the femur and forearm were not affected by calcium therapy.

The results of other trials were positive (Recker et al 1977, Horsman et al 1977, Nordin et al 1980), but calcium therapy was not as effective as physical activity (Smith 1967) or oestrogen therapy (Horsman et al 1977) in the prevention of osteoporosis. In these clinical trials, the techniques for measuring bone mass varied from X-ray morphometry (of doubtful validity) to photon absorptiometry (of a high validity), which could have contributed largely to the different results obtained.

Table 3(iii): Summary of trials on calcium supplementation

Author	Calcium dosage	Site	Bone loss
Recker et al (1977)	1.04 g	hands	retarded
Horsman et al (1977)	800mg	forearm	retarded
Nordin et al (1980)	1.2g	hand,spine	retarded
Lee et al (1981)	719mg	hand	retarded
Smith (1981)	0.75g	forearm	retarded
Riggs (1982)	1.5-2.5g	spine	fewer fractures
Riis et al (1987)	2g	forearm	retarded
Lamke et al (1978)	1g	femur	not retarded
Nilas et al (1984)	500mg	forearm	not retarded
Riis et al (1987)	2g	spine	not retarded

3.3.3 Other nutritional factors

The role of other dietary factors in osteoporosis is less important than the role of calcium. A high protein intake may increase the calcium intake required to maintain a balance (Heany et al 1982). This is physiologically plausible because acid radicals decrease renal tubular reabsorption. Phosphate reduces urinary excretion of calcium but enhances endogenous faecal loss (Heany et al 1982). An increased protein consumption is normally associated with an increase in phosphorus consumption, resulting in a negative calcium balance.

Gallagher et al (1980c) demonstrated that the 1,25 dihydroxy-cholecalciferol level in osteoporotic patients was lower than controls, and Corless et al (1975) showed that very low concentrations of plasma 25-hydroxycholecalciferol were found in patients in a long-stay geriatric hospital. Though vitamin D deficiency results mainly in osteomalacia, a mild deficiency may lead to osteoporosis (Gallagher et al 1974).

3.3.4 Physical activity

The geographical pattern of physical activity overlaps to a large extent with the geographical pattern of osteoporosis. Chalmers and Ho (1970) suggested that hard physical labour might be the factor that protected the Bantu, Singaporean Chinese and Hong Kong Chinese against osteoporosis and proximal femur fractures.

Studies have been performed on groups of subjects exposed to extreme physical conditions. Patients confined to bed and astronauts exposed to weightlessness lose as much as 1 percent of their trabecular bone per week, though this change is reversible (Mazess et al 1983, Whedon 1984). Athletes have more cortical bone in active limbs (Nilsson 1971, Dalen and Olsson 1974, Jones et al 1977, Aloia et al 1978a, Huddleson et al 1980), but young women who become amenorrhoeic from exercise have reduced bone density (Cann et al 1984, Drinkwater et al 1984, Marcus et al 1985).

A number of randomized trials have been conducted on the effects of physical activity on bone density. The effects of physical activity were studied by various techniques: Smith et al (1981, 1984) measured radial bone mineral content, Aloia et al (1978b) measured total body calcium and Krohner and Nielsen (1982) measured lumbar spine bone mineral content. The study by Chow et al (1987) was unique, for bone mass was measured at the hips . A positive effect of exercise on bone density was demonstrated in all studies despite the small sample size.

The effect of physical activities on bone mass is physiologically plausible. Skeletal stresses from weight-bearing and muscle contraction stimulates osteoblastic activity (Riggs et al 1986). As the viability of bone depends on the coupling of the activities of the osteoblasts and osteoclasts, such stimulation from mechanical stress may be vital in maintaining skeletal mass.

At the cellular level, humoral agents which may mediate the action of mechanical stimuli on osteoblasts have also been identified. Experiments showed that prostaglandin E2 was produced when tensile forces were applied to osteoblasts(Yeh and Rodan 1984). Although prostaglandin E2 is a potent bone resorber, it can also enhance bone formation (Smith 1985).

Hence, there is solid evidence on the importance of physical activity in preventing bone loss. Nevertheless, the exact amount and nature of activities required to maintain bone mass is uncertain. Randomized trials on the effects of various forms of exercise on the effects of bone loss among different age groups, for example, the effects of walking exercise in the elderly , are important (Kelsey and Hoffman 1987).

3.3.5 Smoking and alcohol consumption

The relationship between smoking and oestrogen related disease has been thoroughly reviewed by Baron (1984). Four case-control studies were conducted to investigate smoking as a risk factor for osteoporosis (Daniell 1976, Paganini-Hill et al 1981, Kreiger 1982, Williams et al 1982). Paganini et al (1981) and Kreiger (1982) both compared hip fracture patients with controls. Daniell (1976) studied patients with vertebral fractures and Williams et al (1982) included both hip and forearm fractures as cases. Except for the study by Williams et al (1982), all authors demonstrated a relative risk higher than 1 for smoking as a risk factor. Daniell (1976) found a relative risk of 4.3, which was statistically significant. The existing evidence supports smoking as a risk factor for osteoporosis, but the effect of dosage has not been demonstrated with certainty. Such potential confounding factors as age, use of alcohol and oestrogen replacement therapy have not been well controlled in these studies and the estimated relative risks may be inaccurate.

Smoking may cause osteoporosis by inducing an early menopause (Kaufman et al 1980, Williett et al 1983), though Paganini-Hill et al (1981) showed that the age at menopause did not account for the effects of smoking on osteoporosis entirely. Lindsay (1981) reported that the difference in cortical bone mass between female smokers and non-smokers was attributable to the difference in body weight.

Recently smoking has been found to have an important anti-oestrogenic effect by enhancing oestradiol 2-hydroxylation (Michnovicz et al 1986).

Increased ethanol consumption has been shown to be a risk factor for osteoporosis (Nilsson and Westlin 1973, Seeman et al 1983). Ethanol depresses bone formation by a direct effect on the osteoblasts (Baran et al 1980, Farley et al 1985), and has a potential for affecting calcium metabolism in a number of different ways (Aitken 1984 b).

Seeman et al (1983) also showed that the risk of spinal osteoporosis was associated with the amount of alcohol consumed per day and the number of years it has been drunk. A threshold effect has not been demonstrated, and the level of safe consumption is unknown.

3.3.6 Diseases and drug treatments

Diabetes, hyperthyroidism, hyperparathyroidism, Cushing's disease, rheumatoid arthritis, and gastrectomy are some of the medical disorders that have been reported to cause osteoporosis.

A recent study (Hui et al 1985) showed that patients with Type I diabetes had a reduced bone mass, which was not associated with the duration or control of the disease. This was similar to earlier findings by Levin et al (1976) and McNair et al (1978). Nevertheless, Deheeuw and Abs (1977) found that among patients with maturity-onset diabetes, there are two distinct diabetic populations with a small number showing bone loss from the forearm but the majority showing increased bone mass associated with increased body weight. Similarly, Johnston (1985) showed that bone mass is greater in postmenopausal women with Type II diabetes.

Diabetes mellitus may also be a risk factor for hip and other osteoporotic related fractures (Hutchison et al 1979, Paganini-Hill et al 1981). Although this was implied in case-control studies, the results from cohort studies were contradictory(Gallagher et al 1980a, Heath et al 1980).

The use of medications may predispose patients to osteoporosis and/or the susceptibility to falls, and increase the risk of hip fractures. Corticosteroids accelerate trabecular bone loss (Hahn et al 1974, Hahn 1978, Adinoff and Hollister 1983), and thyroid hormone causes reduced cortical bone mass (Ettinger and Wingred 1982). Thiazide diuretics and some psychotropic drugs are associated with an increased incidence of fainting and blackouts and may predispose patients to falls and fractures. In view of the frequency of polypharmacy in the elderly, the role of drugs in proximal femur fractures merits attention.

3.4 Falls and fracture of the proximal femur in the elderly

3.4.1 Falls as a risk factor for fracture of the proximal femur

A tendency to having falls is an important risk factor in fracture of the proximal femur. Aitken (1984a) believed that postural instability was more important than osteoporosis in the aetiology of fracture of the proximal femur, while authors including Nordin (1984) advocated the opposite.

Sheldon (1960) conducted a survey on the factors associated with 500 falls among 202 elderly subjects. He found that women appeared to fall more often than men, that the frequency of falls increased progressively with age, and that 12% of all falls resulted in a femoral neck fracture. Aitken (1984 b) calculated age-specific rates of falls with the number of falls in Wolverhampton and the population in Colchester. He found an exponential rise in the incidence of falls up to the age of 85 years. As the increasing trend towards fractures with age resembled the trend in falls , he postulated that an increase in the frequency of falls might account for an increase in femoral neck fractures with age.

Aitken (1984a) also studied 245 subjects with proximal femur fractures. He found that among both fracture patients and controls, 16% were not osteoporotic. Moreover, the extent of osteoporosis was similar in women with and without a past history of fractures. He concluded that postural instability is the major determinant for femoral neck fractures. It must be pointed out that the patients and controls were from different geographical areas, and bone density was measured by morphometry of the hands and spines rather than the hips.

According to Cooper et al (1987), reduced bone mass was a risk for fracture in subjects below 75 years of age, and above that age neuromuscular responses which protect the skeleton against trauma may be more important.

3.4.2 Epidemiology of falls in the elderly

Falls are a major cause of both mortality and morbidity (Perry 1982)among the elderly, and the cost of treating the condition is high. The prevention of falls is an important aspect for health maintenance in the elderly.

3.4.2.1 Falls as a cause of mortality and morbidity

Accurate incidence data based on prospective studies of representative populations is scarce. The statistics were based on the analysis of hospital data, death certificates and reports of residents in special facilities. Isaacs (1983) quoted the figure determined by

Wild et al (1980) of three million falls among old people in the community and three hundred thousand falls among old people in institutions within a year in the UK. Evans et al (1979) reported thirty thousand falls resulting in fractures of the proximal femur in the UK within a year. According to Melton III and Riggs (1983), a third or more of all elderly individuals in the USA experienced a fall from a standing height each year.

In Canada there were more than 1800 deaths attributed to accidental falls, 72% of which were persons 65 years of age and over (quoted by Gryfe et al 1977). Furthermore, falls are the leading cause of accidental deaths in the home, accounting for two-thirds of such fatalities in persons 65 years of age and over (Metropolitan Life 1973). The severity of the subsequent injuries varies according to the age and sex of the subjects. From 8-40 % of the falls reported resulted in fractures (quoted by Perry 1982). Fracture of the proximal femur was, by far, the most common (Lucht 1971), and the average duration of stay in hospital was as long as 40 days.

3.4.2.2 Circumstances of falls

The incidence of falls rises steeply with age, with the rate of falls increasing exponentially after the age of 75 years (Gryfe et al 1977, Lucht 1971).

The rate of falls are higher in females than in males, at all ages (Lucht 1971, Waller 1974, Gryfe et al 1977). A high proportion of falls occur in the divorced or widowed (Lucht 1971).

Most falls among old people at home occur during daily activities. Falls at night are relatively infrequent (Lucht 1971, Wild et al 1980). Lucht (1971) also showed that the incidence of falls was greatest in the winter months, with a maximum in January. Sheldon (1960) described how 171 accidental falls occurred in 125 individuals from a survey of old people living at home. Slipping contributed to 49 falls and 63 occurred on stairs. Similarly, Lucht (1971) found that slippery surfaces accounted for more than one third of 134 falls, while loose rugs and loose objects were also as dangerous.

To summarize, widowed or divorced elderly women are most susceptible to falls, and environmental factors play a significant role in falls.

3.4.3 Mechanisms of falls and injuries in the elderly

Falls occur when subjects are unable to correct a displacement. There are many factors which can lead to this deficiency in old age. According to Melton III and Riggs (1985), at least half of the falls among elderly people were associated with organic dysfunction, and the proportion increased with age.

Specific diseases may play a role in a minority of falls. These include parkinsonism, strokes, hemiplegia, abnormal cardiac rhythms and conduction defects, pneumonia, arthritis and alcoholism. A much larger proportion of victims suffer from physiological deficits such as diminished postural control, gait changes, muscular weakness, diminished reflexes, poor vision, postural hypotension, vestibular problems, confusion and dementia.

Although most of these diseases cannot be cured, regular physical exercise may improve muscle coordination, reduce the propensity to fall and improve the ability to counteract falls. A hazard-free living environment may also be important in preventing falls.

Risk factors for fracture of the proximal femur in Hong Kong Chinese -a case-control study

4.1 Background and objectives

The incidence of fracture of the proximal femur has been increasing among the elderly in Hong Kong (Chapter 2), but too little is known about the risk factors for effective prevention (Chapter 3).

The objective of this case-control study was to investigate the role of the following risk factors for fracture of the proximal femur in Hong Kong Chinese:

1) Physical inactivity at the time when peak bone mass was reached and in the period before the fracture
2) Low calcium intake
3) Tendency to falls
4) Smoking and alcohol consumption
5) Medical conditions and treatments with a predisposition to osteoporosis and postural instability
6) Early menopause, multiparity and breast feeding

4.2 Methods

4.2.1 Theory and history of case-control studies

In case-control studies, individuals with a particular condition or disease (the cases) are selected for comparison with individuals in whom the condition or disease is absent (the controls). Cases and controls are compared with respect to past exposure to certain risk factors (Schlesselman 1976).

In 1926 Lane-Claypon reported the first case-control study on the role of the reproductive history in the aetiology of breast-cancer. Two case-control studies which linked cigarette smoking with lung cancer were published in 1950 (Levin et al 1950, Wynder et al 1954). The study by Doll and Hill (1952) on lung cancer was a prototype of case-control studies. The methodology of case-control studies was further developed in the 1950's. The most important breakthrough was Cornfield's demonstration (1951) that the exposure frequencies of cases and controls are readily convertible to an estimate of the relative risk, i.e., the ratio of frequency of disease among exposed individuals relative to that among the non-exposed .

The **relative risk** for a risk factor can be defined as the ratio of the incidence of disease in an exposed group to the ratio of incidence of disease in an unexposed group.

Risk factor	Disease		Total at risk
	+ (present)	- (absent)	
+ (present)	A	B	A+B
- (absent)	C	D	C+D
	A+C	B+D	T

In the above table, the relative risk for the risk factor equals $\frac{A/(A+B)}{C/(C+D)}$.

If an event occurs with probability p, then the ratio p/(1-p) is called the odds. For rare diseases, the risk of disease and the odds of disease are almost identical. The ratio of the odds of disease in exposed individual relative to the unexposed is called the **Odds Ratio**. This is AD/BC as shown in the above diagram.

The relative risk has been defined as $\frac{A/(A+B)}{C/(C+D)}$ previously.

If the disease is rare in the population, (A) will be small relative to (B), and the term (A+B) is closely approximated by (B). Similarly, (C+D) is closely approximated by (D).

Hence,

the term $\frac{A/(A+B)}{C/(C+D)}$ is closely approximated by AD/BC. This term is the Odds Ratio, and is the measurement of risk for case-control studies.

4.2.2 Methods of the present study

4.2.2.1 Definition and selection of cases

A case-control method was adopted. Fracture of the proximal femur was defined to include both intertrochanteric and neck fractures (as diagnosed by X-ray and operative findings). Patients with pathological fractures from primary and secondary bone tumours were excluded. From October 1985 to August 1986, 200 consecutive patients were recruited from Kwong Wah Hospital and 200 consecutive patients were recruited from Queen Elizabeth Hospital (Orthopaedic Unit B).

4.2.2.2 Definition and selection of controls

Both hospital and community controls were recruited. Hospital controls were surgical in-patients from the wards of the same hospitals. No diagnostic groups were excluded, and the first surgical patient of the same sex and 5 years-age group (e.g. 50-54, 55-59 etc) admitted after the case was recruited.

For patients older than 70 years, community controls were subjects registered for the Old Age Allowance by the Hong Kong Social Welfare Department. A systematic sample was obtained from the register list for Shatin. Patients from the Chinese University General Practice Unit acted as controls for cases younger than 70 years. In a period of 3 months, all eligible patients attending the general practice clinic were recruited as controls.

All community controls were also matched for sex and five year age group to the patients (e.g. , 50-54, 55-59 etc).

4.2.2.3 The interview and the questionnaire

The mental status of the patients was checked by testing his or her orientation in time, place and person. Only patients who were orientated and could recall their names, age and addresses correctly were interviewed. The patients and controls were interviewed by one of two trained female interviewers using a standardized, structured questionnaire (Appendix I). Each interviewer was responsible for interviewing all patients and controls from the same hospital, and the community control for the case. The questionnaire included few open ended questions, in order to reduce the variability of responses by the elderly. It was designed to describe the demographic background of patients and controls, a history of falls and mobility before the fracture, current and past physical activity level, current calcium intake, smoking, alcohol consumption, medical and drug history and reproductive history (Appendix I).

All patients who were considered unsuitable for recruitment due to a poor mental state or other reasons were seen by the principal investigator. This was to assess the completeness of case ascertainment and to document the reasons for unsuccessful interviews. A systematic sample which included 10 % of patients, 10% of hospital controls and 10% of community controls were also interviewed by the principal investigator to study the validity of ascertainment by interviewers.

The physical activity levels in the period before the fracture and at age 30 years were measured by asking the subjects to report the frequency with which five forms of activities were performed in a week. Only activities which are commonly performed in the every day life of elderly Chinese subjects were included, and only activities which involved weight-bearing at the hips were chosen. Recreational activities were not included in the list o past and current activities, for there was evidence that a very small percentage of the population was engaged in recreational sports activities (Millar 1979).

The current activity level was classified as highest if subjects performed one of these forms of activity daily: walking uphill, walking with a load, walking upstairs (at least three flights); intermediate if subjects walked on the streets every day, and lowest if otherwise. The past activity was high if the subjects walked uphill or with a load every day in the past, and low if otherwise. These levels were used in the conditional logistic regression analysis.

To assess the levels of calcium intake, the subjects were questioned on the frequency with which nine local food items were consumed. These foods were the major source of calcium in the Chinese diet (Ho, 1988). The average weekly calcium intake was calculated by using the South East Asian Food Composition table (USA Department of Health, Education and Welfare, 1972) to determine the calcium content of the average portion size of nine foods, and multiplying this content by the frequency of consumption (every day=7/week, on alternate days=3.5/week, once to twice weekly=1.5/week, occasionally or never=0/week). The average daily consumption was derived from the average weekly consumption.

The quintiles of calcium intake for the whole population of patients and controls were calculated and the odds ratio for the different quintiles of calcium intakes were calculated using the number of patients and controls distributed in each quintile.

4.2.2.4 Sample size calculation

In a matched case-control study, the total number of pairs of patients and controls can be estimated from the predetermined level of significance, power, and percentage of controls exposed.

M = total number of pairs of cases and controls required

$$M = \frac{m}{(P_oQ_1 + P_1Q_o)} \quad \text{........... formula 1}$$

P_o = estimated proportion of controls exposed to the risk factor of interest

$Q_o = (1 - P_o)$

P_1 = estimated proportion of cases exposed to the risk factor of interest

$$= \frac{P_o R}{[1 + P_o(R - 1)]}$$ (where R denotes the smallest relative risk of interest)

$$Q_1 = (1 - P_1)$$

m is given by the formula:

$$m = \frac{[Z_\alpha/2 + Z_\beta\sqrt{P(1 - P)}]^2}{(P - {}^1/_2)^2}$$ .... formula 2

Z_α = standard normal deviate corresponding to the chosen level of significance
= 1.96 for a p-value of 0.05

Z_β = standard normal deviate corresponding to the chosen power
= 1.58 for a power of 90%

$$P = \frac{\text{relative risk}}{1 + \text{relative risk}}$$

Assuming a relative risk of 2, and choosing α as 5%, the power as 90% (β = 10%) and using formula 2, m = 90.

Assuming 10% of the controls are exposed to the risk factors, and using formula 1

M = 368.

Hence at the 95% level of significance, 368 pairs of cases and controls are required to detect an odds ratio of 2 with 90% power.
(Reference: Schlesselman, 1982, p.161)

4.2.3 Statistical Methods

4.2.3.1 Logistic regression

For case-control studies, the odds ratio can be calculated from either conventional maximum likelihood methods or by the more recently developed logistic regression techniques .

Conditional logistic regression is the standard technique for matched case-control studies. This method was used to calculate the odds ratio (a close approximation of the relative risk) throughout the analysis. The methodology as described in the textbook by Breslow and Day (1980) is used as a reference.

The name logistic regression originated from the fact that the *logit* transformation of the probability of disease in each risk category is expressed as a linear function of *regression* variables whose values correspond to the levels of exposure to the risk factors.

That is, if P denotes the probability of disease associated with being exposed to x.

$$\text{Logit } P = \ln \left[\frac{P}{1-P} \right] = \alpha + \beta x$$

(Where ln stands for natural logarithm)

If there is exposure to 2 factors x_1 and x_2

$$\text{Logit } P(x_1\, x_2) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_1 x_2$$

Here β_1 represents the natural log (ln) relative risk for being exposed to x_1, β_2 represents the ln relative risk for being exposed to x_2 and β_3 for being exposed to both.

The odds ratios calculated in logistic regression are adjusted for exposure to other risk factors in the same model.

In the situation where controls are matched to cases in a 1:1 or 1:M manner, **conditional logistic regression** is applied. The theory and computation are similar to logistic regression, but the odds ratios are calculated within matched sets.

Conditional logistic regression was performed by the package EGRET. This programme utilizes the method of maximum likelihood estimation to calculate the odds ratio and its confidence intervals. The significance of a single risk factor is evaluated from the log-likelihood statistic of a model containing the risk factor as the sole independent variable. The significance of additional risk factors is similarly evaluated from the change in the log-likelihood statistic after the risk factors are added as an independent variable in the model.

When more than one risk factor is used as the independent variables in the same logistic model, the odds ratios derived are adjusted odds ratios. This enables adjustment for confounding effects. One can test for a trend in risk with increasing dose exposure, by using coded levels of exposure. The logic and results are similar to a x^2 test for trend.

The interaction between two risk factors can be investigated in logistic regression by first fitting a model with the two risk factors, and then extending the model by the inclusion of an interaction term (i.e. $x_1 x_2$ in the above equation). The change in the log-likelihood statistic follows the chi-square distribution and the corresponding p-value is an indication of the statistical significance of the interaction.

4.2.3.2 Other statistical tests used in the study

1. The two-sample median test

The median test is a non-parametric procedure for testing whether two samples differ in central tendencies. A 2x2 contingency table with counts of the number of cases and controls greater than the median or less than and equal to the median for the cases and controls as a group is compiled. A chi-square test is then performed for the 2x2 contingency table.

This test was used for comparing the median age at menarche and menopause, the number of pregnancies and children born and breast-fed for cases and controls. (SPSS User's Guide 1983, p.685).

2. The t-test and the chi-square test

The paired t-test was use to compare the mean calcium intake between patients and controls, and the chi-square test was used to investigate the association between a history of stroke, physical activity and a history of falls.

4.2.3.3 Calculation of the attributable risk

The attributable risk is the maximum proportion of a disease that can be attributed to an aetiological factor (Lilienfeld and Lilienfeld 1980).

$$\text{Attributable Risk (AR)} = \frac{b(r-1)}{b(r-1)+1} \times 100 \quad \text{(Levin 1953)}$$

where b = proportion of the population with the aetiological factor

r = relative risk (or odds ratio)

In this study the attributable risk for the various risk factors was calculated using the odds ratio as an estimate of the relative risk and the prevalence of risk factors among the controls as an estimate of the proportion of the population with the aetiological factor.

4.3 Results

4.3.1. Response rate and demographic data

Four-hundred fifty-nine patients had to be recruited to obtain four hundred valid interviews. The reasons for unsuccessful interviews are presented in Table 4 (i). Four percent of the patients were not orientated in time, place and person or could not recall their names, age and addresses correctly. Another 4 % spoke unknown dialects or claimed that they could not hear the interviewers' questions. Only 3 % of the patients were discharged, transferred or deceased prior to the interview. A total of 445 hospital controls and 408 community controls were approached to complete 400 valid interviews in each group.

Table 4 (i): Reasons for unsuccessful interviews

	Number	%
Completed	400	87
Refused	8	2
Confused or demented	18	4
Language or hearing problem	17	4
Discharged, transferred or deceased	16	3
Total	459	100

The age and sex distribution for patients is shown in Table 4 (ii). The female patients were much older than the male patients. Thirty-nine percent of the men were less than 70 years old while 42% of women were 80 years and over.

Table 4 (ii): Age and sex distribution of patients

Age(Years)	Male	Female
less than 70	47 (39%)	54 (19%)
70 - 79	45 (37%)	108 (39%)
eighty and over	28 (24%)	118 (42%)
Total	120 (100%)	280 (100%)

4.3.2 Description of the falls and the fractures

4.3.2.1 Types of fractures

Forty percent of the men and 61% of the women were diagnosed as having cervical fractures. The rest had intertrochanteric fractures.

4.3.2.2 The sites and the time at which fractures occurred

Most of the falls and the fractures happended at home (38% for men and 51% for women); and on the streets (27% for men and 17% for women) (Table 4 iii).

Some of the falls and fractures occurred in subway stations, public toilets, restaurants and in buses, and were classified into the 'others' category in Table 4 (iii).

Table 4 (iii): Sites at which fractures occurred

Place	Male	Female
Workplace	14 (12%)	2 (1%)
Home	45 (38%)	135 (48%)
Housing block	7 (6%)	34 (12%)
Market	2 (2%)	7 (3%)
Street	32 (27%)	46 (16%)
Others	16 (13%)	36 (13%)
Don't know	4 (3%)	20 (7%)
Total	120 (100%)	280 (100%)

The approximate time when the fracture occurred is shown in Table 4 (iv). A substantial proportion of men and women could not recall the exact time when the fracture. occurred. Of those who knew, most fell in the daytime .

Table 4 (iv): Time at which fractures occurred

Time	Male	Female
7 - 12am	30 (25%)	109 (39%)
1-8pm	38 (32%)	89 (32%)
9pm-6am	15 (13%)	32 (11%)
Don't know	37 (31%)	50 (18%)
Total	120 (100%)	280 (100%)

4.3.2.3 Activities predisposing subjects to fractures

The activities during which the fractures occurred are shown in Table 4(v). Most of the fractures seemed to occur with minor trauma. For example, more than 20% of the fractures occurred while subjects were standing up or sitting down, and about half resulted from falling on level ground.

Table 4(v): Activities engaged in when fractures occurred

Activity	Male		Female	
Standing up/sitting down	35	(29%)	74	(26%)
Walking on level ground	59	(49%)	143	(51%)
Walking up and down slopes	2	(2%)	1	(0%)
Falling down one or more flight of stairs	15	(13%)	33	(12%)
Running	0	(0%)	3	(1%)
Traffic accident	4	(3%)	4	(1%)
Others	1	(1%)	0	(0%)
Don't know	4	(3%)	22	(8%)
Total	120	(100%)	280	(100%)

4.3.3 Risk factors

4.3.3.1 Physical activity

There was little correlation between the current and past levels of physical activity of subjects: the Spearman rank correlation coefficient was 0.16 both for walking uphill and walking with a load.

Most of the responses for the frequency of activity fell into the 'every day' or 'never' category, for example, 68% of patients walked on the streets every day, and 83% never walked with a load. The odds ratios for not performing the various forms of load-bearing activities daily (currently and in the past) were higher than one, although only the differences between patients and community controls were statistically significant (Table 4 (vi) a).

Table 4(vi)a: Physical activity and risk of fracture

Activity	No. of Patients (n=400)	Hospital controls OR (95% CI)	Community controls OR (95% CI)
Current			
Walking on streets every day	270	1.0(-)	1.0(-)
Not walking on streets every day	130	1.5(1.0-2.1)	1.8(1.3-2.6)
Walking upstairs every day	146	1.0(-)	1.0(-)
Not walking upstairs every day	253	1.3(1.0-1.8)	1.3(1.0-1.8)
Walking uphill every day	22	1.0(-)	1.0(-)
Not walking uphill every day	278	1.7(1.0-3.4)	1.3(0.6-2.5)
Walking with a load every day	20	1.0(-)	1.0(-)
Not walking with a load every day	379	1.2(0.6-2.5)	2.2(1.2-4.0)
Past			
Walking uphill every day	328	1.0(-)	1.0(-)
Not walking uphill every day	72	1.1(0.8-1.6)	2.0(1.4-2.7)
Carrying a load every day	164	1.0(-)	1.0(-)
Not carrying a load every day	235	1.3(1.0-1.8)	1.2(0.9-1.7)

The odds ratios were higher in women than in men for all current activities, except for not walking with a load every day in the past (Table 4 (vi)b). This indicated that daily load-bearing activity in the period preceding the fracture and in the past was associated with a reduction in the risk of a fracture.

Table 4(vi)b: Physical activity and the risk of fracture by sex

Activity	Men		Women	
	No. of patients (n = 120)	*OR (95%C.I.)	No. of patients (n = 280)	*OR (95%C.I.)
Current				
Not walking on streets every day	25	1.3 (0.8-2.4)	105	1.7 (1.2-2.3)
Not walking upstairs every day	71	1.2 (0.7-1.8)	182	1.4 (1.0-1.9)
Not walking uphill every day	111	1.4 (0.6-3.2)	267	1.5 (0.7-2.9)
Not walking with a load every day	111	1.4 (0.5-2.9)	268	2.1 (1.1-4.1)
Past				
Not walking uphill every day	19	1.5 (0.8-2.8)	53	1.6 (1.1-2.2)
Not walking with load every day	38	1.6 (1.0-2.6)	126	1.2 (0.9-1.5)

* Odds Ratio for performing activities daily as 1.0, and matching 2 controls to 1 case.

For men and women who were younger than 70 years old, the odds ratio for not performing most forms of load-bearing activities was not higher than 1. Contrarily, the odds ratios were higher than 1 for the older age groups. Thirteen percent of patients younger than 70 years, 25% of patients 70 to 79 years, and 49 % of patients 80 years and above did not walk every day.

Table 4(vi)c: Physical activity and the risk of fracture by age groups

	Odds Ratio* (95% C.I.) for the different age-groups		
Activity	younger than 70 years	70 to 79 years	80 years and above
Current			
Not walking on streets every day	2.0 (0.9-4.3)	1.3 (0.8-2.0)	1.8 (1.2-2.7)
Not walking upstairs every day	0.9 (0.6-1.5)	1.4 (0.9-2.1)	1.6 (1.1-2.5)
Not walking uphill every day	0.9 (0.3-2.2)	2.0 (0.9-4.3)	1.4 (0.4-4.3)
Not walking with a load every day	0.5 (0.2-1.1)	6.0 (2.2-17.0)	2.0 (0.2-17.9)
Past			
Not walking uphill every day	0.9 (0.4-1.7)	2.4 (1.5-3.8)	1.3 (0.8-2.1)
Not walking with a load every day	0.8 (0.5-1.4)	1.8 (1.2-2.6)	1.2 (0.8-1.8)

* Odds ratio for performing activities daily as 1.0

The odds ratio increased as the level of load-bearing activity decreased, and the trend was statistically significant (Table 4(vi)d).

Table 4 (vi)d: The risk of fracture for different levels of load-bearing activities

Level of activity	No. of Patients (n = 400)	Odds Ratio (95% C.I.)	
I. Load-bearing activity daily	160	1.0	(-)
II. Walking daily	116	1.2	(0.8-1.5)
III. Not walking daily	124	1.7	(1.1-2.1)
Test for trend		P less than 0.05	

4.3.3.2 Dietary calcium intake

The frequencies with which fractured proximal femur patients consumed various foods containing calcium are presented in Table 4(vii)a. The pattern of consumption was generally similar for both patients and controls. Dairy products were very infrequently consumed. The main source of calcium in the subjects' diet was from the consumption of green vegetables. A smaller fraction was from small fish, soya bean products, and bread products.

Table 4 (viia): Frequency of consumption of various food items by fractured proximal femur patients

Food Item	Frequency of consumption		
	Daily	At least once weekly	Occasionally or never
Milk	9%	7%	84%
Milky drinks	4%	4%	82%
Milk in tea/coffee	8%	3%	89%
Cheese	0%	2%	98%
Soya bean curd	3%	25%	72%
Soya bean milk	1%	7%	82%
Small fish	3%	14%	83%
Green vegetables	79%	14%	7%
Bread or cakes	29%	21%	50%

The dietary calcium intake, as crudely approximated by the calcium index, was much lower than the Recommended Dietary Allowance for Caucasians (Heany et al 1982). The mean calcium indices for patients, hospital controls and community controls are shown in Table 4(vii)b. The calcium intake of patients was consistently lower than both control groups, and all the differences were statistically significant at the 0.05 level except for female patients and hospital controls.

Table 4(viib): Means and standard deviations of calcium intake in patients and controls

	Patients	Hospital Controls	Community Controls
Men	127.93 (99.13)	168.42 (143.88)*	168.01 (142.12)*
Women	140.60 (121.45)	157.99 (135.29)**	195.72 (169.20)***

* p = 0.01 between patients and controls by paired t-test
** p = 0.1 between patients and controls by paired t-test
*** p = 0.001 between patients and controls by paired t-test

Due to the method of dietary assessment, some subjects had exactly the same calcium intake. The quintiles of calcium intake was calculated, but the proportion of subjects in each quintile was not exactly one-fifth, for many subjects had a similar calcium intake.

The odds ratio for fractures of the proximal femur in each quintile of calcium intake was calculated, using an intake higher than or equal to 244 mg as the baseline for comparison. For both hospital and community controls, the odds ratio for fracture of the proximal femur increased with a low calcium intake (Table 4 vii c). This trend was statistically significant, indicating a dosage effect.

Table 4(viic): Quintiles of calcium intake and the isk of fracture

Quintiles of calcium intake (mg/day)	Number of subjects in quintile patients (n = 400)	hospital controls (n = 400)	community controls (n = 400)	Odds Ratio (95% CI) (compared with highest quintile) hospital controls		community controls	
≥ 244	60	82	97	1.0	(-)	1.0	(-)
129-	74	79	87	1.3	(0.8-2.2)	1.4	(0.9-2.2)
83 -	65	66	83	1.9	(1.1-3.2)	1.7	(1.0-2.9)
75-	61	45	57	1.9	(1.1-3.2)	1.7	(1.0-2.9)
< 75	137	128	76	1.5	(0.9-2.3)	2.9	(1.9-4.6)
Test for trend				p = 0.05		p < 0.001	

There was an increasing risk of fracture of the proximal femur with decreasing calcium intake in both men and women (table 4(vii)d). The odds ratio for the lowest quintile of calcium intake was 1.9 in women and 2.0 in men.

Table 4 (vii)d: Quintiles of calcium intake and the risk of fracture by sex

Quintiles of calcium intake (mg/day)	Odds Ratio (95% C.I.) Men		Women	
≥ 244	1.0	(-)	1.0	(-)
129-	1.5	(0.7-3.1)	1.3	(0.8-2.0)
83 -	1.6	(0.8-3.2)	1.1	(0.7-1.9)
75-	1.4	(0.6-3.2)	1.8	(1.1-3.0)
< 75	2.0	(1.0-3.7)	1.9	(1.2-2.9)
Test for trend	p = 0.05		p < 0.001	

4.3.3.3 Susceptibility to falls

Fifty-eight per cent of patients, 63% of hospital controls and 55% of community controls were able to go out of home without any aid before the fracture, the odds ratio for being unable to mobilize out of home without an aid was 0.9(95 % C.I. 0.6-1.2) for community controls and 1.3(95 % C.I. 0.9-1.8) for hospital controls.

A total of 20 per cent of patients, 12 per cent of hospital controls and 13 per cent of community controls had a history of falls in the previous year. About one third of those who fell consulted a western style practitioner.

The odds ratio for a history of falls in the past year was 1.9 (95% C.I.=1.2-2.9) for hospital controls and 1.8 (95% C.I.=1.2-2.7) for community controls. There was little difference between the sexes, the odds ratio being 1.7(95%CI =0.8-3.3) for men and 1.9(95% CI=1.3-2.7) for women.

The relationship in different age groups is shown in Table 4 (viii). A tendency to fall was a significant risk factor only in subjects younger than 70 years old. It can be seen from Table 4(viii) that there was a rapid increase in the number of control subjects who had a history of falls with increasing age. As a result, the difference between patients and controls was highest in the youngest age group.

Table 4(viii): History of falls in the preceding year and the risk of fracture

Age group	Odds Ratio* (95% C.I.)	% of subjects with a history of falls: Patients	% of subjects with a history of falls: Controls
younger than 70	4.1 (1.8-9.0)	19%	5%
70-79	1.9 (1.1-3.2)	20%	14%
older than 80	1.3 (0.8-2.1)	23%	19%

* The odds ratio for no history of falls as 1

Moreover, more of the patients had a history of fractures in the preceding five years than the controls (10%, 3% and 4% in patients, hospital controls and community controls respectively). The odds ratio for a history of a fracture in preceding five years was 4.4 (95% C.I.=1.9-10.1) for hospital controls and 3.1 (95% C.I.=1.5-6.4) for community controls. In 41 fractures sustained by the subjects, 19 were fractures of the femur, six were fractures of the vertebrae and eight were a fractures of the forearm.

4.3.3.4 Smoking and drinking alcohol

The odds ratio for smoking was 1.6 (95%CI=1.1-2.3) for comparison with hospital controls and 1.8 (95%CI=0.8-1.5) for comparison with community controls. In men, 77% of patients, 59% of hospital controls and 70% of community controls were smokers or ex-smokers.

In women, 26% of the patients, 21% of the hospital controls and 26% of community controls were smokers or ex-smokers. The odds ratio for being a smoker or an ex-smoker was significant only in men (Table 4(ix).

Table 4(ix): Smoking, alcohol consumption and the risk of fracture

Factor	Men		Women	
	No. of patients (n=120)	*OR (95%C.I.)	No. of patients (n=280)	*OR(95%C. I.)
Smoker or ex-smoker	92	1.9 (1.1-3.1)	73	1.1 (0.8-1.6)
Drinking every day	31	3.6 (1.9-6.7)	11	4.8 (1.7-13.6)

* The odds ratio for nonsmoker as 1 and not drinking alcohol every day as one.

Though only 26% of the men and 4% of the women among the patients reported that they drank every day, an elevated risk was demonstrated in both groups (Table 4 ix). Only eight patients, eight hospital controls and three community controls admitted that they had ever been hospitalized for drinking problems.

4.3.3.5 Medical conditions and drug treatments

A history of a stroke was associated with an increased risk of fracture Table 4(x). There was no significant increase in risk for the other diseases or drug treatments. The odds ratio for a history of a stroke was 4.6 (95% CI =2.2-9.6) for women and 2.1 (95% CI= 0.8-5.5) for men.

Table 4(x): Medical and drug history and the risk of fracture

Medical and drug history	Hospital controls (OR±95% CI)	Community controls (OR±95% CI)	No. of patients with a positive history (n = 400)
A history of:			
Stroke	2.3 (1.0-5.0)	5.4 (1.8-19.1)	28
Diabetes mellitus	1.2 (0.7-2.2)	1.8 (0.9-3.4)	36
Thyroid disease	1.6 (0.6-4.3)	2.1 (0.8-6.6)	16
Renal disease	2.0 (0.6-7.0)	12.0 (1.4 - f)	12
Heart disease	0.8 (0.5-1.2)	1.4 (0.8-2.6)	40
Hypertension	1.1 (0.8-1.7)	1.0 (0.7-1.5)	12
On drugs for:			
Heart disease	0.8 (0.4-1.6)	1.0 (0.5-2.0)	20
Hypertension	0.9 (0.6-1.4)	0.9 (0.6-1.4)	56
Sedation	1.1 (0.4-3.6)	1.8 (0.5-7.5)	8

The activity level and a history of falls for fracture patients with and without a history of stroke is shown in Table 4(xia) and 4(xib). Patients who had suffered a stroke walked outdoors less often than patients without a history of a stroke. There was no association between a history of a stroke and a history of falls in the past year.

Table 4(xi)a: Activity level of patients with proximal femur fractures, and with and without a history of stroke

	Walk on street every day	Not walk on street every day	Total
A history of a stroke	13	15	28
No history of a stroke	255	113	368
Total	268	128	396

Chi-square value = 5.2, degrees of freedom = 1
p-value = 0.02

Table 4(xi)b: Relationship between a history of a stroke and falls among patients with proximal femur fractures

	A history of falls	No history of falls	Total
A history of a stroke	7	21	28
No history of a stroke	75	293	368
Total	82	314	396

Chi-square value = 0.1, degrees of freedom = 1
p-value = 0.73

4.3.3.6 Reproductive factors

The median and mean for the age of menarche and menopause was very close. The median age of menarche and menopause for patients, community controls and hospital controls was very similar. Nevertheless, more patients had given birth to and breast-fed two or more children than the controls (Table 4 xii).

A total of eight patients, five hospital controls and seven community controls had undergone oophorectomy. Oestrogen replacement for menopause was uncommon, only three patients, two hospital controls and two community controls claimed that they were given 'special drugs' during their menopause.

Table 4(xii): Reproductive history for patients and controls

Factor	Patients Median	Hospital controls Median	Community controls Median
Age at menarche	16	16	16
Age at menopause	47	48	48
No. of pregnancies	3	4	2
No. of live births	3	3	2*
No. of children breast-fed	2	2	1*

* The medians for the number of live births and number of children breast-fed were two, and more of the patients had more than two children born and breast-fed than the community controls (p less than 0.05 by the median test).

4.3.4. Results of conditional logistic regression

4.3.4.1 Confounding effects

The result of Logistic Regression (using 1 case and 2 controls in a matched set) is shown in Table 4(xiii). The first column of Table 4(xiii) shows the odds ratio for each risk factor used singly as the independent variable in a model. The second column shows the odds ratio for these risk factors when they were all included as the independent variables in the same model. The adjusted odds ratios in the second column were similar to the unadjusted odds ratios in the first column, indicating that the effects of the risk factor was quite independent of each others i.e. an absence of confounding effects.

Table 4(xiii): Results of conditional logistic regression by univariate and multivariate analyses

Risk Factor	Odds Ratio (95% CI) One independent variable		Odds Ratio (95% CI) Multiple Regression	
Current physical activity				
Highest level	1.0	(-)	1.0	(-)
Intermediate level	1.2	(0.9-1.6)	1.2	(0.9-1.6)
Lowest level	1.8	(1.3-2.4)	1.6	(1.2-2.3)
Calcium score				
Highest quintile	1.0	(-)	1.0	(-)
Fourth quintile	1.3	(0.9-2.0)	1.2	(0.8-1.8)
Third quintile	1.3	(0.8-1.9)	1.2	(0.8-1.9)
Second quintile	1.7	(1.1-2.6)	1.7	(1.1.-2.7)
Lowest quintile	1.9	(1.3-2.7)	1.9	(1.3-2.7)
Smoking				
Non-smoker	1.0	(-)	1.0	(-)
Smoker or ex-smoker	1.3	(1.0-1.7)	1.3	(0.9-1.7)
Alcohol consumption				
Not drink every day	1.0	(-)	1.0	(-)
Drinking every day	3.9	(2.3-6.7)	4.0	(2.3-7.0)
Falls in previous year				
No history of a fall	1.0	(-)	1.0	(-)
History of a fall	1.8	(1.3-2.5)	1.8	(1.2-2.4)
A history of a stroke				
No	1.0	(-)	1.0	(-)
Yes	3.5	(2.0-6.2)	3.2	(1.8-5.8)

4.3.4.2 Interaction effects

The statistical significance of the interaction between various risk factors is shown in Table 4(xiv). None of the interaction between the various risk factors was significant.

Table 4(xiv) Statistical significance (P-values) of the interaction between risk factors

	Calcium intake	Smoking	Alcohol consumption
Current activity	0.6	0.7	0.3
Calcium intake	-	0.2	0.6
Smoking	-	-	0.5

4.3.4.3 Attributable risks

The attributable risks based on the odds ratio obtained from the multiple regression model are presented in Table 4(xv). These are only approximations because odds ratios were used instead of relative risks. Moreover, the prevalence of risk factors was not estimated from a random sample of the population. Approximately 13% of all fractures were attributed to physical inactivity and 19% to a low calcium intake, indicating that these are important factors for prevention. For a history of falls in the previous year, the attributable risk was 9%. The attributable risk will be much smaller if a more stringent definition of susceptibility to falls was used, with a smaller prevalence. Although the odds ratio for drinking and smoking was 4.0 and 3.2 respectively, the attributable risk was low due to a low prevalence.

Table 4 (xv): Attributable risks for the various factors

Factor	Odds Ratio	Prevalence in all controls	Attributable risk
Lowest level of physical activity	1.7	0.22	13%
Lowest quintile of calcium intake	1.9	0.26	19%
History of falls	1.8	0.12	9%
Drinking alcohol every day	4.0	0.03	8%
History of a stroke	3.2	0.02	4%

4.3.5 Comparison of results with other studies

There are many studies on the risk factors for osteoporosis, however it is appropriate to compare our results with case-control studies only. The results from other case-control studies are tabulated here, and further discussed in the discussion section.

Table 4(xvi) Physical activity and the risk of fracture of the proximal femur

Author/Year	No. of patients/ controls	Levels of activity	Odds Ratio (95% C.I.) Women	Men
Lau, 1988	400/800	I. Load-bearing daily	1.0 (-)	1.0 (-)
		II. Walking daily	1.1 (0.8-1.7)	1.3 (0.8-2.1)
		III. Walking less than daily	2.0 (1.4-2.8)	1.2 (0.6-2.3)
Cooper, 1988	300/600	I. Load-bearing several times a day	1.0 (-)	1.0 (-)
		II. Weekly to daily	1.0 (0.6-1.8)	3.6 (1.0-12.9)
		III. Less than weekly	1.7 (1.0-3.1)	5.6 (1.3-23.9)
		IV. Never	1.7 (1.0-3.1)	2.5 (0.5-13.2)

Table 4(xvii) Calcium intake and the risk of fracture of the proximal femur

Quintiles of Calcium intake		Lau, 1988 (400 patients, 800 controls) women (OR±95%CI)	men (OR±95%CI)	Cooper, 1988 (300 patients, 600 controls) women (OR±95%CI)	men (OR±95%CI)
Highest	I	1.0 (-)	1.0 (-)	1.0 (-)	1.0 (-)
	II	1.2 (0.8-2.0)	1.5 (0.7-3.2)	1.2 (0.7-2.1)	6.2 (1.2-32.7)
	III	1.1 (0.7-1.9)	1.7 (0.8-3.7)	1.1 (0.6-2.0)	3.3 (0.8-14.1)
	IV	1.9 (1.2-2.9)	1.4 (0.6-3.4)	1.4 (0.8-2.5)	5.8 (1.1-29.0)
Lower	V	1.9 (1.2-2.9)	2.1 (1.1-4.2)	1.2 (0.7-2.2)	6.2 (1.3-29.7)

Table 4(xviii) Smoking and the risk of fracture of the proximal femur

Author/Year	no. of patients/ controls	Contrast	Odds Ratio (p-value)
Lau, 1988	400/800	ever smoker/never smoker	1.0 ($p>0.05$)
Cooper, 1988	300/600	ever smoker/never smoker	1.7 ($p<0.05$)
Paganini-Hill, 1976	91/182	≥ 11 cigs. per day/none	2.0 ($p>0.05$)
Kreiger, 1982	98/884	ever smoker/never smoker	1.0 ($p>0.05$)
Williams, 1982	160/6606	ever smoker/never smoker	*

* Odds ratios were significantly higher in smoker for most weight and oestrogen-user groups.

Table 4(xix) Reproductive history and the risk of fracture of the proximal femur

	High parity	Prolonged breast-feeding	Early menopause
Lau, 1988	increased risk	increased risk	not associated
Kreiger, 1982	not associated	decreased risk	not associated
Wyshak, 1981	decreased risk	not studied	not studied

Table 4(xx) History of falls and the risk of hip fracture

Author/Year	Findings
Lau, 1988	The odds ratio was 3.2 (95% C.I. 1.8-5.8) for a history of falls in the last year.
Cooper, 1988	The odds ratio was 1.8 (95% C.I. 1.3-2.5) for a history of falls in the last 9 months
Cook, 1982	A significantly higher proportion of patients reported falls in the last year than controls ($p<0.001$ by x^2 test).

4.4 Discussion

4.4.1 Study design and sources of bias

This case-control study was designed to assess risks in a retrospective manner. The sources of bias in case-control studies have been comprehensively enumerated by Schlesselman (1982).

In this study incident patients admitted to two major hospitals for proximal femur fractures were recruited. The response rate was fairly high, very few patients were deceased before the interview, and only a few subjects could not be interviewed because of a poor physical or mental state. The reasons for unsuccessful interviews were confirmed by the principal investigator (see methods), and no patients were excluded for convenience or other invalid reasons. As patients who had died or who were demented could not be interviewed, the recruited patients may represent a 'healthier' sample of all patients with hip fracture. This may lead to a slight under estimation in relative risk between risk factors and hip fracture, but will not cause a falsely high relative risk.

The recall bias was probably more important for some risk factors than others. For example, patients may have been more likely to report a history of falls in the past than the controls. Nevertheless, the other risk factors for fracture of the proximal femur and osteoporosis are not well-known in the local population, and the association of such factors as a lack of physical activity and low calcium intake with fracture of the proximal femur was unlikely to be due solely to recall bias.

The major potential source of bias was the selection of controls. Many of the community controls lived at home or in institutions designed for individuals who were capable of self-care. They represented a 'healthier' sector of the elderly who could have been physically more active and following a better diet. On the other hand, hospital controls had diseases which could have been indirectly a cause or a result of physical inactivity and a meagre diet. Despite the different backgrounds of the 2 control groups, similar differences were found between the patients and both groups. Though there was a larger difference between patients and community controls, all the differences was along the same lines.

The community controls were recruited from Shatin while the patients lived in Kowloon. The possibility that there might be some systematic difference in life-styles between these groups were considered. The results of a health survey conducted in the urban area of the whole of Hong Kong (the Biosocial Survey conducted in 1979; Millar 1979) was compared with the results from a health survey conducted in Shatin (the Shatin Survey conducted in 1983; Donnan 1988). The lifes-tyles of the two groups were very similar. For example, 24% of the elderly men in urban areas and 23% of the elderly men in Shatin exercised outdoors at least once per week. The corresponding percentages for elderly women were 8% in Kowloon and 7% in Shatin. The percentage of elderly men and women who smoked and regularly drank alcohol were also similar in the two surveys. This background suggested that the observed differences between hip fracture patients and community controls in our study could not be accounted for by a systematic difference in life-styles of subjects from these two areas.

The whole of Hong Kong lies within one degree of latitude, and variation in climate between Shatin and Kowloon is negligible. Although there is some difference in the living environment, the results of the two surveys mentioned previously showed that the stress experienced by the residents of the two areas was similar. As measured by the Langer scale, 26% of the elderly men and 40% of the elderly women exhibited some psychophysiological maladjustment in the urban area (Biosocial survey conducted in 1979; Millar 1979). The corresponding figures were 26% in men and 49% in women in Shatin (Shatin Survey conducted in 1983; Donnan 1988).

The inclusion of hospital controls who lived in the same areas as the patients enabled comparison within the same residential area. As the same differences were observed between patients and both control groups, with only a difference in the magnitude of the relative risk, this further supported the validity of the findings.

4.4.2 Discussion of results

This study was designed to document the relative importance of the risk factors for fracture of the proximal femur in Hong Kong Chinese, rather than to quantify such risk factors as calcium intake or physical activity. The risk factors found to be important included physical inactivity, a low calcium intake, a history of falls in the previous year, drinking alcohol and smoking, and a history of a stroke. The effects of the risk factors were independent, for very few changes were observed in the relative risk after adjustment by multiple logistic regression.

4.4.2.1 Physical activity

In this study it was clearly demonstrated that regular load-bearing activities were associated with a reduced risk of proximal femur fractures. The protective role of various load-bearing activities was particularly important in subjects 80 years of age and above. This has not been shown clearly in past intrapopulation studies. A recent randomized trial by Chow et al (1987) showed that aerobic exercise had a positive effect on hip bone mass in postmenopausal women. Chalmers and Ho (1970) first postulated that hard physical labour protected Chinese women against hip fractures. The dietary calcium intake has always been low in Hong Kong Chinese, but due to urbanization, there has been a reduction in physical activity by the general population. Recreational activities are also limited by space limitations. A lack of physical activity is the factor that can best account for the dramatic increase in the incidence of proximal femur fractures over the last twenty years.

The effects of physical activity on bone mass are physiologically plausible. Skeletal stresses from weight-bearing and muscle contraction stimulate osteoblastic function (Riggs et al 1986). At the cellular level, prostaglandin E2 was isolated as a mediator of the response to physical stress, and mechanical forces can increase its production in bone-cell cultures (Somjen et al 1986).

It is commonly accepted that exercise is beneficial in an aging population. Bortz(1980) recently reviewed the biological changes that occur during the aging process in the various systems of the human body. He concluded that at least a portion of the aging changes are due to physical inactivity, which can be improved by a continuing programme of physical exercise (Bortz 1980). Of the different types of exercise, walking has been highly recommended for the elderly (Council on Scientific Affairs, American Medical Association 1984). Walking is easily practised by elderly Chinese who are not used to other recreational activities. The effects of regular walking exercise on bone mass and hip fractures should be evaluated by controlled trials.

4.4.2.2 Calcium intake

The mean calcium intake in Chinese was much lower than the Recommended Dietary Intake of one gram, and this is supported by the results of another study conducted in Hong Kong (Ho 1988). The main source of calcium in the Chinese diet was from green vegetables, soya products and fish. Dairy products are infrequently consumed by elderly Chinese. It was postulated that lactase deficiency was prevalent among Chinese, and this was the reason for the low milk consumption (Pun 1987). There is little epidemiological evidence to support this, and cultural factors may account largely for the rarity with which dairy products are consumed. Knowledge of the reasons for this is an important basis for dietary advice .

In addition to the low dietary intake, the bioavailability from the sources of calcium in the Chinese diet may be low. For example, calcium from green vegetable are of a low bioavailability (Pun 1987). The most effective and efficient way to increase calcium intake may be in the form of calcium supplements.

Many clinical trials conducted in Caucasians have showed a small positive effect of calcium supplements on bone mass and the rate of bone loss (Recker et al 1977, Horsman et al 1977, Nordin et al 1980). These studies were conducted in population where the average calcium intake was much higher than in Hong Kong. Calcium supplements could be more effective in preventing osteoporosis in Hong Kong Chinese than in other populations, and randomized trials are essential.

4.4.2.3 Susceptibility to falls

Postural instability and susceptibility to falls could not be measured in an objective manner because of the retrospective nature of the study. A history of falls in the year preceding the fracture was taken. This was subjected to considerable recall bias as patients who fracture their hips might recall more falls. Nevertheless a statistically significant odds ratio was not obtained in all age groups. This indicated that the high odds ratio was not due solely to bias. Another indicator of the tendency to falls was a history of fractures in the preceding five years. The odds ratio for a history of fracture was three for both control groups, indicating that the patients were frequent fallers and were more susceptible to fractures.

A tendency to falls seemed to be an important risk factor in subjects younger than 80 years. The frequency of falls in the elderly rises exponentially with age (Aitken 1984 a), and the difference between patients and controls is much smaller in the older age groups. According to Evans (1982) and Cooper et al (1987), the ability of the neuromuscular response to counteract falls may be a more important determinant of hip fracture than the liability to falls in subjects older than 75 years. This may apply to our population, and may account for the observed age difference.

The intrinsic and extrinsic risk factors for falls in the elderly have been well reviewed by Peck (1986). Only a limited number of these factors are amenable to prevention. It is obvious that the environment should be modified, and such drugs as sedatives and antihypertensives should not be prescribed indiscriminately. Nevertheless, hearing loss and decreased visual acuity with aging are irreversible changes. The importance of physical activities has been discussed, and its potential in preventing falls should add to its merit. Regular activity can increase muscle strength, improve co-ordination and improve confidence in walking. This is important in preventing falls and the 'post-fall syndrome' (Murphy and Isaac 1982) in the elderly.

4.4.2.4 Smoking and alcohol consumption

Smoking and drinking alcohol every day were risk factors for proximal femur fractures in men. Smoking induces an early menopause (Kaufman et al 1980, Williett et al 1983), and this is the most likely mechanism by which smoking causes osteoporosis. Paganini-Hill et al (1981) showed that the age at menopause did not account for the effects of smoking on osteoporosis entirely, and Lindsay (1981) reported that the differences in cortical bone mass between female smokers and non-smokers was attributable to the differences in body weight.

Recently, smoking has been found to have an important anti-oestrogenic effect by enhancing estradiol 2-hydroxylation (Michnovicz et al , 1986).

Alcohol suppresses osteoblasts (Baran et al 1980, Farley et al 1985) and may predispose drinkers to falls (Peck 1986). Increased ethanol consumption has been shown to be a risk factor for osteoporosis (Nilsson and Westlin 1973, Seeman et al 1983). Seeman et al (1983) also showed that the risk of spinal osteoporosis was associated with ounces of alcohol consumed per day, years of drinking, and ounce-years. A threshold effect has not been demonstrated, and the cutoff for safe consumption is unknown.

4.4.2.5 Medical conditions and drug treatments

Contrary to findings in the West, most diseases and drug treatments have not been found to be risk factors for proximal femur fractures in elderly Chinese.

Strokes are common in elderly Chinese, and it has been demonstrated that this is a risk factor for fracture of the proximal femur. As many as 7% of 400 hip fracture patients had a history of stroke in the past. Patients with a history of proximal femur fractures and a stroke walked on the streets less frequently than patients without such histories. Early mobilization and active rehabilitation are important for stroke patients.

4.4.2.6 Reproductive factors

The patients had more children and had breast-fed more children than the community controls. This contradicted findings by Smith (1967), Daniell (1976), and Aloia et al(1983). Multiparity and breast-feeding might have accentuated the already low calcium intake in the Chinese women, and may predispose them to osteoporosis by a negative effect on bone mass.

There was a lack of consistency in the difference in number of children born and breast-fed between patients, hospital controls and community controls. Though the median number of children born and breast-fed by the patients was slightly higher than the community controls, this did not lend any evidence for multiparity and breast-feeding as risk factors for fracture of the proximal femur.

4.4.2.7 Attributable risks

The attributable risk is the percentage of disease risk that is attributable to individual risk factors. For example, it can be seen that about 13% of the risk of hip fracture was attributable to lack of load-bearing activities, and 19% was attributable to a low calcium intake. Although the calculated attributable risks are only approximations (for reasons as presented in the methods section), these indicated that in general, physical inactivity and a low calcium intake are important risk factors for fracture prevention.

Vitamin D concentration and blood biochemistry in patients with proximal femur fractures in Hong Kong

5.1 Vitamin D deficiency and its significance

Vitamin D deficiency is common among elderly populations living in a temperate climate (McKenna et al 1985). A low vitamin D level is also associated with fracture of the proximal femur. Ulivieri et al (1986) compared hip fracture patients and patients with vertebral fractures. He found that both the serum 25-hydroxycholecalciferol and the urinary calcium were lower in patients with fracture of the proximal femur. This confirmed earlier findings by Lips et al (1982), Hoikka et al (1982), Baker et al (1979) and Baylink et al (1977). The vitamin D levels in fracture of the proximal femur patients have not been studied in Asians living in a tropical climate.

The biochemical indices of bone metabolism were also measured in some studies conducted in Europe and North America. Hoikka et al (1982) concluded that hypocalcaemia and increased alkaline phosphatase levels were frequent in fracture of the proximal femur patients, but both Ulivieri et al (1986) and Lips et al (1982) did not find any significant difference in the serum alkaline phosphatase, calcium or phosphate levels.

The plasma 25-hydroxyvitamin D (25-OH(D)) level is frequently used as an index of vitamin D supply, for this is the most abundant circulating metabolite (Preece et al 1975). The total body store of vitamin D depends on cutaneous production as well as on dietary intake. In the elderly, plasma 25-OH(D) correlates more strongly with exposure to sunlight than with dietary intake (Hodkinson et al 1973).

It is well-known that severe and prolonged vitamin D deficiency cause cause osteomalacia. Subclinical vitamin D deficiency can play a role in the pathogenesis of osteoporosis (Parfitt et al 1982), and this is of importance to public health.

5.2 Objectives

The objectives of this study were to investigate the role of a low vitamin D level as a risk factor for fracture of the proximal femur in Hong Kong Chinese, and to study the blood biochemistry of patients with a low vitamin D level.

5.3 Subjects and Methods

The vitamin D level and blood biochemistry were studied in the two hundred patients who were subjects of the case-control study conducted in Queen Elizabeth Hospital as described in Chapter 4 (age range=49-93 years). On admission, venous blood was taken for measuring 25-hydroxyvitamin D (25-OH(D)) and serum albumin, calcium, phosphate and alkaline phosphatase (from February to November in 1986).

The control subjects were four hundred and twenty-seven subjects living in government flats for the elderly. They were participants in a survey of the elderly (age range 60-90 years). Venous blood was also taken for measuring 25-hydroxyvitamin D and biochemical assays (from June to November in 1986).

Serum calcium, phosphate, alkaline phosphatase and albumin level were measured by standard laboratory techniques on an American Monitor Parallel Analyser (American Monitor USA).

The albumin-adjusted calcium levels were derived by the following formula (Payne et al 1973):-

Albumin-adjusted calcium concentration

= measured calcium concentration+ 0.025 (40-albumin concentration)

An aliquot of serum was stored at -70 degrees C for assay of 25-OH(D) by competitive protein-binding assay as previously described (MacDonald and Swaminathan 1988). Serum was mixed with acetonitrile and centrifuged. The supernatant was applied to a Sep Pak C18 cartridge (Waters Associates USA) which had been prepared by washing with acetonitrile and water. The cartridge was then washed with water and methanol. The 25-OH(D) was then eluted with acetonitrile, and dried under nitrogen. The extract was stored under nitrogen at -20 degrees C until assay, which was performed within two days. Recovery of the extraction was monitored for each specimen by adding a small amount of labelled 25-OH(D) to the sample, and this ranged from 60% - 80%.

The extracts were reconstituted in ethanol and assayed by a competitive protein binding method using plasma from a vitamin D deficient pig at a dilution of 1 in 4000. All values were individually corrected for losses throughout the whole procedure. The interassay coefficient of variation was 6.9%.

The normal ranges for the plasma 25-OH(D), albumin-adjusted calcium, phosphate and alkaline phosphatase were calculated from the mean and sample standard deviation of the controls. The t-test was used for comparing means and proportions between patients and controls.

The mean serum 25-hydroxyvitamin D level for the controls was compared with values from various temperate countries as quoted by McKenna et al (1985). The original

25-OHD levels were converted from nmol/L to μg/L by multiplying by a factor of 0.4 (Bouillon et al 1986).

5.4 Results

Table 5(i) shows the mean 25-OH(D) level by sex and age. In all groups, the levels were lower in the hip fracture patients than the controls (p less than 0.0001 by the student's t-test). Moreover, in the patients, the 25-OH(D) level was lower in women than in men (p less than 0.01 by the student's t-test). There was no statistically significant difference between patients in different age-groups (p larger than 0.05 by the student's t-test).

Table 5(i): Serum 25-hydroxy vitamin D concentration in patients and controls (in μg/L)

	Serum 25-hydroxyvitamin D Mean (S.D.)(number of subjects in group)					
	Patients			Controls		
Men younger than 70 years	22.5	(7.2)	(n=28)	33.9	(10.2)	(n=63)
Men 70 years and over	18.5	(6.9)	(n=32)	32.2	(8.6)	(n=90)
Women younger than 70 years	17.8	(5.5)	(n=31)	29.0	(6.2)	(n=81)
Women 70 years and over	17.1	(6.2)	(n=107)	26.0	(6.8)	(n=134)

The vitamin D level was lower in patients than controls at the 0.001 level for all groups

Twenty percent of the male patients and 30% of the female patients had a 25-OH(D) level below the 95% confidence limit of the controls. The normal 95% confidence limits for men were 14.6-51.3 μg/L and for females were 13.7-40.3 μg/L. Most of the subjects with abnormal 25-OH(D) levels were very old; of men 78% and of women 68% were 80 years and over.

The mean 25-OHD level in the controls was higher than levels from healthy old people living in temperate countries, but was similar to the figure from Australia (Table 5(ii)).

Table 5(ii): Serum 25 (OH)D levels in temperate countries, Australia and Hong Kong

Author	Country	Mean 25 (OH)D level in μg/L
Von Knorring (1982)	Finland	6.8
Schmidt-Gayk (1977)	West Germany	8.4
McKenna (1985)	Ireland	8.4
Lester (1977)	United Kingdom	8.6
Rapin (1982)	Switzerland	9.2
Chapuy (1983)	France	11.9
Omdahl (1982)	USA	12.4
Lund (1975)	Denmark	22.0
Tassie (1985)	Australia	27.2
This study	Hong Kong	27.0

Table 5(iii) shows the plasma calcium (albumin-adjusted), phosphate, and alkaline phosphatase concentration in patients and controls. There were no statistically significant differences in calcium and alkaline phosphatase concentration between patients and controls, but the serum phosphate was significantly higher in patients than controls for both sexes (p less than 0.01).

Table 5 (iii): Blood biochemistry of patients and controls (means and standard deviations)

Serum concentrations	Men		Women	
	Patients	Controls	Patients	Controls
Calcium (in mmol/L)	2.29(0.13)	2.28(0.11)	2.31(0.12)	2.29(0.12)
Phosphate level (in mmol/L)	1.01(0.24)	0.84(0.17)	1.10(0.19)	0.97(0.15)
Alkaline Phosphatase (in IU/L)	107.3(45.3)	113.5(26.7)	105.4(37.5)	113.3(33.8)

Of all patients with a lower 25-OH(D), none had a biochemical picture suggestive of osteomalacia. Only one man and two women had an elevated serum alkaline phosphatase level (upper limit for men=157 IU/L and for women = 180 IU/L). None of the subjects with a low 25-OH(D) level had an albumin-adjusted calcium and serum phosphate level outside the normal range (the normal range for albumin-adjusted calcium was 2.06-2.50 and 2.05-2.53 mmol/L for men and women respectively; the normal range for phosphate was 0.5-1.13 and 0.67-1.34 mmol/L for men and women respectively).

Hip fracture patients with low 25-OH(D) levels were less ambulant than patients with a normal level. In patients with a low level, only 33% reported that they could walk outdoors without any aids, and 30% never walked outdoors. For hip fracture patients with a normal vitamin D level, 61% could walk outdoors without any aids and only 8% said they never walked outdoors. These proportions were statistically significant at the 0.01% level by the t-test.

5.5 Discussion

5.5.1 Effects of stress on vitamin D level

In this study, a low 25-hydroxyvitamin D level was observed in hip fracture patients. As subjects with hip fractures have been under stress due to the fall and the fracture, the effects of stress on these measurements must be considered before concluding that a low vitamin D level is of aetiological importance in fracture of the proximal femur.

Cooper et al (1989) studied the serum concentration of 25-hydroxyvitamin D and other biochemical indices of bone metabolism in women with hip fracture. Two control groups were recruited: in-patient controls and out-patient controls. All the in-patient controls were admitted for acute disease such as bronchopneumonia, cardiac failure, stroke and urinary tract infection. The inclusion of this control group enabled a comparison of vitamin D level and blood biochemistry of hip fracture patients with a group that was similarly under the stress of illness. The results of the study is shown here:-

Table 5(iv): Study by Cooper et al (1989): Biochemical values (mean and SD) in patients with hip fractures and control groups

	Hip fractures	In-patient controls	Out-patient controls	Laboratory ref. range
Number	41	20	20	
Age (years)	77.4 (8.6)	73.3 (10.5)	66.9 (11.8)	
Albumin (g/l)	30.1 (3.7) [a]	34.7 (3.4)	38.1 (2.6)	32-50
Serum creatinine (µmol/l)	110.0 (39)	105.0 (28)	84.0 (22)	60-125
Calcium (mmol)	2.3 (0.17)	2.4 (0.16)	2.4 (0.13)	2.15-2.55
Alkaline phosphatase (IU/l)	234.0 (184)	192.0 (55)	190.0 (93)	100-350
25(OH)D (µg/l)	9.4 (5.8) [a]	14.3 (9.4)	19.4 (10)	4-40
PTH (µg/l)	0.4 (0.18)	0.4 (0.21)	0.3 (0.12)	<0.5
Osteocalcin (ng/ml)	11.8 (13.4) [b]	15.9 (7.6)	13.6 (12.7)	8-36
Urine OHPro/Cr (µmol/mmol)	14.8 (7.9)		15.7 (13.4)	<30

a Significantly lower in fracture patients ($p<0.001$) after ANOVA with age as the covariate.

b When log transformed, significantly lower in fracture patients than in-patient controls after ANOVA with age as the covariate ($p<0.02$)

The results indicated that the 25(OH)D level was significantly lower in hip fracture patients than both control groups. Moreover, when the lower limit for serum 25(OH)D level was set at 8 µg/L , 49 percent of the hip fracture patients were vitamin D deficient, as compared with 15% of in-patients and 10% of out-patient controls.

The magnitude of the difference in vitamin D levels between patients and controls in this study resembles that between patients and out-patient controls in Cooper's study. Such a difference is unlikely to be due to stress alone, but rather to a genuine vitamin D deficiency status in hip fracture patients.

The effects of certain hormones on 25-hydroxyvitamin D level have also been studied. Nielsen (1980) administered 40mg of prednisone daily for 5 days to 'normal' subjects. The serum 25-hydroxyvitamin D level remained unchanged. This suggested that the 25-hydroxyvitamin D level is not readily affected by extrinsic hormones.

5.5.2 Significance of results

The vitamin D level for both patients and controls was measured in the same laboratory and by the same technician, and the difference was unlikely to be due to inter-laboratory or inter-observer variation. Though the winter is mild in Hong Kong (average temperature about 17 degrees C, with sunshine on most days), a small seasonal variation has been observed in medical students (MacDonald and Swaminathan 1987) and infants (Leung unpublished data). Here the period of study for both subjects and controls did not include the winter months of December and January, and the difference was much larger than previously observed. Hence it is likely that a genuine difference in serum vitamin D levels existed between patients and controls.

The 25-OHD level in control subjects indicated a good vitamin D nutrition status when a comparison was made with populations living in a temperate climate (Table 5(ii)). The latitude range for these temperate countries was 35 to 60 degrees, while Hong Kong lies 22.5 Degrees north of the Equator. Much of the difference in vitamin D level was probably due to a difference in the intensity of solar radiation. The lower 25-OHD level in the hip fracture patients compared to the local controls demonstrated in this study are in accordance with other studies conducted in Europe (Lips et al 1982, Hoikka et al 1982, Ulivieri et al 1986). Though the vitamin D nutrition status is good in the general population, a low vitamin D level is a risk factor for hip fractures in Hong Kong.

None of the patients with a low vitamin D level had a blood picture suggestive of frank osteomalacia. This is in accordance with the studies by Uliveri et al (1986) and Lips et al (1982), which failed to demonstrate any difference in serum calcium, phosphate and alkaline phosphatase level between patients and controls. However, the study by Hoikka et al (1982) showed a difference in serum calcium and alkaline phosphatase levels between patients and controls.

The use of biochemical criteria (i.e. a lowered serum calcium and phosphate level, and an elevated alkaline phosphatase level) to diagnose osteomalacia is of doubtful validity. It has been demonstrated that biochemical tests may be normal in osteomalacia (Anderson et al 1966, Jenkins et al 1973, Daw et al 1979, Eid 1978), and a diagnosis of osteomalacia should be made by histology.

5.5.3 Effects of a low vitamin D level

In some studies vitamin D deficiency had led to histologically confirmed osteomalacia in fracture of the proximal femur patients (Hoikka et al 1982). However, the results of most investigations showed that a mild vitamin D deficiency did not lead to osteomalacia (Lips et al 1982, Hogervorst et al 1985).

There are other mechanisms whereby vitamin D deficiency can lead to hip fractures. Mild vitamin D deficiency has been shown to lead to bone resorption and osteoporosis (Baylink et al 1977). Vitamin D deficiency may cause muscle weakness and a tendency to falls, which is an important risk factor for hip fracture (Melton III and Riggs 1983). Finally, the blood vitamin D level may not be a direct antecedent of hip fractures, but may be a non-specific indicator of physical inactivity and poor nutrition, which can cause hip fracture.

5.5.4 Prevention of vitamin D deficiency

The main sources of vitamin D in human subjects are dietary intake and skin synthesis. In the elderly, the plasma 25-hydroxycholecalciferol level correlates more strongly with sunlight exposure than with dietary vitamin D intake (Hodkinson et al 1973, Lips et al 1987). Most vitamin D rich foods such as fatty fish, eggs and chicken liver are seldom consumed by elderly Chinese, who eat mainly vegetables, lean meat and rice. A change in dietary habits will be difficult to maintain in elderly Chinese and is of doubtful value in the prevention of vitamin D deficiency.

The vitamin D nutrition status was good in the controls, and the low vitamin D level in fracture of the proximal femur patients was probably due to an inadequate exposure to sunlight because of their reduced mobility. As reported here, a large percentage of subjects reported that they never walk outdoors. It has been demonstrated previously that regular load-bearing exercise protects against hip fractures. Hence, outdoor exercise programmes may maintain vitamin D levels, increase bone mass and prevent hip fracture in the elderly.

Determinants of bone density in elderly Chinese

6.1 Introduction

The relationship between bone density and proximal femur fractures has been discussed in chapter 3. Osteoporosis is generally accepted as the most important cause of hip fractures (Consensus Development Conference 1987), but it has also been claimed that osteoporosis has little aetiological relation to such fractures (Evans et al 1981, Wicks et al 1982, Aitken 1984a, Cummings 1985).

In a recent longitudinal study conducted by Riggs et al (1988), bone density at the hip was found to be directly related to the risk of fractures, with a fracture threshold at about 1 g/cm^2. Hence it is important to study the determinants of bone density at the hip, so that insight can be gained into the risk factors for osteoporosis and hip fractures. Preventive measures can be based on such knowledge.

The various studies on the relationship between determinants and bone density have been summarised in Chapter 3 of this thesis. Stevenson et al (1989) recently found that being thin, drinking, smoking, nulliparity, no oral contraceptive use, and inactivity affect bone density adversely in premenopausal women. An adequate calcium intake and physical activity were important determinants of radial bone mass in premenopausal women (Halioua, 1989).

The determinants of bone density at the hip and spine in elderly Chinese were studied and are presented. Dual X-ray densitometry was used to measure bone density at the hip and spine.

6.2 Objectives

The objectives were to study the determinants of bone density at the hip and spine in elderly Chinese women. These determinants were:-

- anthropometric measurements - height, weight and body mass index
- past and current physical activity level
- past pattern of dairy product consumption and current calcium intake
- reproductive history including age at menopause, history of oophorectomy, parity and history of oral contraceptive use.
- current mental function
- medical conditions which include diabetes mellitus and thyroid disorder, use of diuretics and steroids
- history of a hip fracture

6.3 Methods

6.3.1 Population studied

A cluster sample of elderly women from an old age hostel were studied. All subjects were independent in self-care. Two women with breast cancer and one with leukaemia were excluded from the study. One woman suffered from hyperparathyroidism, and was excluded from the final analysis, leaving a total of 80 subjects in this study.

6.3.2 Questionnaire for assessing the determinants of bone density

A standardized questionnaire was administered by the principal investigator (EMCL) and a research nurse to the women (Appendix I b)

The current calcium intake for the women who cooked their own meals was assessed by a food diary for three consecutive days. All meals were weighed by the research nurse. The calcium intake was then calculated using calcium contents derived from the South-East Asian Food Composition Table. The average daily calcium intake was then calculated. The calcium intake of subjects who consumed hostel food was assessed by weighing all meals supplied by the hostel over three consecutive days. The daily calcium intake was the average intake over the three days.

Mental status was assessed by a brief questionnaire adapted from Hodkinson (1972). A total of eight questions were used. One mark was assigned for each correct answer and none for an incorrect answer.

6.3.3 Measurements of bone density

Bone mineral density was measured by a dual energy X-ray densitometer (X-26 machine manufactured by Norland Incorp.). The bone mineral density was measured at three sites in the left hip (neck, intertrochanteric area, Ward's triangle) and at the L_2 - L_4 level of the spine. For subjects with a history of a hip fracture, bone density was measured at the contralateral hip.

All measurements were conducted by the same trained technician and supervised by the principal investigator (EMCL).

The height of all subjects was measured without shoes, and the weight of all subjects was measured with the subjects wearing a shirt and light pants.

6.3.4 Statistical Methods

Correlation was used to study the association between bone density at various sites and between numerical determinants and bone density. Regression was used to study the relationship between the dependent variables (i.e. bone density) and the independent variables (i.e. the determinants of bone density).

The t-test was used to compare the bone density of subjects in different risk categories. Analysis of covariance was used to adjust for the effects of other determinants when categorical determinants was studied; and multiple regression were used for studying the effects of two or more independent numerical variables.

Stepwise (a combination of step-up and step-down technique in SPSS) multiple regression was used to generate best-fitting models which account for most of the variation in bone density at the various sites.

6.4 Results

6.4.1 Relationship between bone density at various sites

Table 6(i) shows the mean and standard deviation of bone density at three sites in the hip and spine. The bone density at the intertrochanteric area, neck area and Ward's triangle are highly correlated. The bone density at various sites were also correlated with bone density at the L_2 - L_4 spine.

Table 6(i). Descriptive statistics of bone density and the correlation coefficient (r) at various sites.

Site	Mean ± (SD) g/cm^2		Correlation Coefficient (r)		
			Intertrochanteric	Wards Triangle	L_2 - L_4
Neck	0.53	(0.09)	0.77	0.75	0.49
Intertrochanteric	0.45	(0.09)	-	0.74	0.60
Ward's Triangle	0.48	(0.10)	-	-	0.42
L_2 - L_4 Spine	0.70	(0.14)	-	-	-

* All the correlation coefficients were statistically significant at the 0.001 level.

6.4.2 Categorical determinants of bone density

The subjects were from 62 to 92 years old, and the mean age was 76 years. Table 6(ii) shows the mean, standard deviation and results of the t-test comparing the bone density of subjects exposed and not exposed to these factors: smoking, drinking, sedentary occupations, no regular milk intake in the past, nulliparous, diabetes mellitus and hip fracture.

Eleven subjects had known diabetes mellitus. The mean bone density of these subjects was high at all sites (P less than 0.05 by the t-test). The mean body mass index of subjects with diabetes mellitus was 23.8 kg/m^2(SD=3.9 kg/m^2) and for non-diabetic subjects was 22.5 kg/m^2 (SD=4.5 kg/m^2) (p value > 0.05 by t-test). The difference in bone density at the hip (neck and intertrochanteric) area remained statistically significant after adjusting for the body mass index (by ANCOVA).

Only four subjects had consumed dairy products regularly in the past. The bone density at the femoral neck and trochanteric region was higher in these subjects than women who did not report a regular milk (or cheese) consumption .

Seven subjects had a history of a hip fracture. The bone density at the femoral neck and Ward's Triangle in these subjects were lower than the rest. The mean age for subjects with and without a history of a hip fracture was 76.6 and 77.5 years respectively. The mean mental test score for subjects with a hip fracture was 3.1 (SD=1.3) and for subjects without hip fracture was 4.7 (SD=1.5) (P<0.001 by t-test). The mean body mass index for subjects without a hip fracture was 22.9 kg/m^2 (SD=4.6 kg/m^2) and for subjects with a hip fracture was 20.5 kg/m^2 (SD=2.9 kg/m^2) (p>0.05 by t-test). The difference in bone density at the femoral neck and Ward's triangle became statistically non-significant after adjusting for the mental test score and body mass index.

No subjects suffered from thyroid disease. Five subjects were on diurectics, but the bone density of these subjects were not significantly different from the others.

Twenty-eight subjects were nulliparous, but there was no significant difference in bone density between these women and others who had given birth to children. Six subjects had a history of oophorectomy, but these women did not have a lower bone density. Oral contraceptive or postmenopausal oestrogen replacements had not been used by any of the 80 women.

Table 6(ii) Bone density (means and standard deviations) (in g/cm^2) in women with or without a positive history of diabetes mellitus, past active job, past regular milk and cheese consumption, childbirth, smoking and drinking alcohol

Site	Factor	Positive	Negative
	DIABETES MELLITUS	(N = 11)	(N = 69)
Femoral Neck		0.59 (0.09)	0.52 (0.08)*
Ward's Triangle		0.52 (0.10)	0.48 (0.12)*
Trochanteric Region		0.51 (0.09)	0.44 (0.09)*
Spine L_2 - L_4		0.79 (0.20)	0.68 (0.12)*
	SELDOM DRINK SMILK AT AGE 30 YEARS	(N = 76)	(N = 4)
Femoral Neck		0.53 (0.09)	0.62 (0.06)*
Ward's Triangle		0.49 (0.12)	0.53 (0.12)
Trochanteric Region		0.45 (0.09)	0.54 (0.13)*
Spine L_2 - L_4		0.69 (0.13)	0.80 (0.24)
	HIP FRACTURES	(N = 7)	(N = 73)
Femoral Neck		0.47 (0.07)	0.54 (0.09)*
Ward's Triangle		0.37 (0.08)	0.49 (0.12)*
Trochanteric Region		0.40 (0.07)	0.46 (0.09)
Spine L_2 - L_4		0.66 (0.10)	0.70 (0.14)
	ON DIURETICS	(N = 5)	(N = 75)
Femoral Neck		0.54 (0.13)	0.53 (0.08)
Ward's Triangle		0.50 (0.18)	0.48 (0.12)
Trochanteric Region		0.42 (0.11)	0.46 (0.09)
Spine L_2 - L_4		0.73 (0.18)	0.69 (0.14)
	SMOKING	(N = 27)	(N = 53)
Femoral Neck		0.52 (0.06)	0.54 (0.10)
Ward's Triangle		0.48 (0.10)	0.49 (0.13)
Trochanteric Region		0.45 (0.09)	0.46 (0.10)
Spine L_2 - L_4		0.68 (0.12)	0.70 (0.15)
	DRINKING ALCOHOL	(N = 12)	(N = 68)
Femoral Neck		0.55 (0.11)	0.53 (0.08)
Ward's Triangle		0.51 (0.13)	0.48 (0.12)
Trochanteric Region		0.50 (0.12)	0.45 (0.09)
Spine L_2 - L_4		0.70 (0.12)	0.70 (0.14)
	PAST SEDENTARY JOB	(N = 37)	(N = 43)
Femoral Neck		0.54 (0.08)	0.53 (0.09)
Ward's Triangle		0.48 (0.12)	0.49 (0.12)
Trochanteric Region		0.45 (0.10)	0.45 (0.09)
Spine L_2 - L_4		0.71 (0.13)	0.69 (0.15)
	NULLIPAROUS	(N = 28)	(N = 52)
Femoral Neck		0.51 (0.11)	0.53 (0.09)
Ward's Triangle		0.57 (0.16)	0.48 (0.12)
Trochanteric Region		0.47 (0.13)	0.45 (0.09)
Spine L_2 - L_4		0.67 (0.12)	0.70 (0.14)

* The mean bone density of the 2 groups differ significantly ($p<0.05$) by t-test.

6.4.3 Numerical determinants of bone density

In these elderly women (age range 62 to 92 years), bone density at the hip was negatively correlated with age. Nevertheless, there was no association between bone density at the spine and age. At the hip, bone density decreased by 0.005 at the femoral neck and 0.009 at the Ward's Triangle every year.

Both the body weight and the body mass index (Wt/Ht^2) was positively correlated with bone density at both the hip and spine. When the body mass index increased by 1 unit, the bone density increased by 0.007 at the femoral neck and 0.01 g/cm^2 at the spine. There was little change in the regression coefficients and their statistical significance after adjusting for age and diabetic status.

There was also a significant positive correlation between the mental test score and the bone density at the hip. As the mental test score increases by one the bone density increases by 0.02 to 0.03 g/cm^2 at the hip. There was little change in the regression coefficients after adjusting for age. Nevertheless, bone density at the spine was not significantly associated with the mental test score.

For activities at 30 years, 58 percent of all women reported that they walked with a load less than once a week and a similar percentage said that they worked actively while standing less than once a week. Thirty-five percent of all subjects claimed that they never walked outdoors currently while 20% walked outdoors daily. There was no statistically significant correlation between past and current activity scores (the total hours spent in load bearing activities) and bone density at the hip or spine.

Thirty-two subjects cooked for themselves, and their average calcium intake was 266 mg (standard deviation = 82 mg). The calcium content of the hostel food was 250 mg per day. There was no significant association between current calcium intake and bone density at the hip or spine.

Table 6(iii). Relationship between determinants of bone density and bone density at various sites

Site	Age	Weight	Height	BMI (kg/m²)	Mental test score	Calcium intake (n=31)	Current activity score	Past activity score	Age at menopause
FEMORAL NECK									
r	-0.31**	0.48**	0.24	0.36**	0.38**	0.03	0.18	0.01	0.1
R	-0.005**	0.004**	0.30+	0.007**	0.02*	-	-	-	-
TROCHANTERIC AREA									
r	-0.29**	0.5***	0.22	0.43**	0.29*	0.09	0.2	0.03	0.06
R	-0.006**	0.005**	0.28	0.009**	0.02*	-	-	-	-
WARD'S TRIANGLE									
r	-0.44**	0.42*	0.19	0.32*	0.37**	-0.07	0.01	0.04	0.2
R	-0.009**	0.005**	0.33	0.009**	0.03**	-	-	-	-
SPINE (L_2 - L_4)									
r	-0.09	0.39**	0.14	0.33*	0.160	0.05	0.09	-0.2	0.05
R	-0.002	0.006**	0.28	0.01*	0.014	-	-	-	-

r = correlation coefficient
R = regression coefficient (presented for significantly correlated determinant only)
+ = $p < 0.05$
* = $p < 0.01$
** = $p < 0.001$

6.4.4 Results of multiple regression

As shown in Table 6(iv), in the multiple regression models with the best fit , 33% of the variance in bone density at the neck of femur, 30% at the intertrochanteric area and 18% at the Ward's Triangle were accounted for. Age, body mass index, mental score and diabetic status were found to be significant predictors of bone density at all sites at the hip (except diabetic status which was not a predictor of bone density at the Ward's Triangle).

In contrast, a combination of the determinants could only account for 16% of variance for bone density at the spine. The only significant predictors were body mass index and the diabetic status.

Table 6(iv). Stepwise regression models for bone density

1. Bone density at the femoral neck

Predictor variable	Regression coefficient	P-value
Mental test score	0.016	0.03
Body mass index	0.005	0.003
Age	-0.004	0.007
Being diabetic	0.082	0.007
Sum of squares due to regression		0.23
Residual sum of squares		0.36
$F = 12.6$; $p < 0.0001$		

2. Bone density at the intertrochanteric area

Predictor variable	Regression coefficient	P-value
Mental test score	0.01	0.05
Body mass index	0.008	< 0.0001
Age	-0.005	0.008
Being diabetic	0.07	0.008
Sum of squares due to regression		0.23
Residual sum of squares		0.43
$F = 10.3$; $p < 0.0001$		

3. Bone density at the Ward's triangle

Predictor Variable	Regression coefficient	P-value
Mental test score	0.02	0.02
Body mass index	0.007	0.003
Age	-0.007	0.0006
Sum of squares due to regression		0.37
Residual sum of squares		0.76
$F = 12.6$; $p < 0.0001$		

4. Bone density at L_2 - L_4 of the spine

Predictor Variable	Regression coefficient	P-value
Body Mass Index	0.01	0.004
Being a Diabetic	0.09	0.03
Sum of squares due to regression		0.25
Residual sum of squares		1.30
$F = 7.5$; $p < 0.001$		

6.5 Discussion

6.5.1 Bone density at various sites

In this study, bone density was measured by a precise method. Dual X-Ray absorptiometry has much better precision (CV=<1%) than dual-photon absorptiometry (CV=1 to 2%) (Goldsmith MF 1989).

The bone density measurements at all sites in the hip were highly correlated, the correlation coefficients being about 0.75. Moreover, the bone density at the spine was associated with bone density at the hip, the correlation coefficients being higher than 0.4. Although the proportions of trabecular bone varies in the different sites at the hip and the spine (50% in the trochanteric region, 25% in the neck, and >66% in the spine) (Cummings 1985), the bone density was highly correlated.

Elderly women were found to lose little or no cortical bone (Mazess 1982, Hui et al 1982). However, age was found to be an important determinant of bone density here. On average, the bone density decrease by 0.005g/cm^2 in the femoral neck and 0.002g/cm^2 in the spine every year. Although bone density at the spine decreased with age, the decrease was much smaller and was not statistically significant. This reflected the different pattern of bone loss in postmenopausal and senile osteoporosis. As more than 66% of the spine is trabecular bone (Riggs 1985), and much trabecular bone is lost immediately after the menopause, the decrease in bone density with age was slight. On the other hand, hip bone is comprised of 50% cortical and 50% trabecular bone. As senile osteoporosis affects both cortical and trabecular bone, a significant amount of bone is lost with aging. Our observation seemed to have confirmed the existence of the two forms of osteoporosis: postmenopausal osteoporosis and senile osteoporosis(Albright 1947, Riggs and Melton 1983).

6.5.2 Diabetes mellitus

The bone density of diabetic patients was higher at both the hip and the spine than other subjects in this survey. The effect of diabetes on bone density is independent ofthe body mass index.

The published data on the relationship between diabetes mellitus, insulin level and bone density at various sites are inconclusive. Levin (et al 1976) reported that bone mass at the forearm was lower for both juvenile and adult-onset diabetics. Deheeuw and Abs(1977) found that in maturity onset diabetics, there are two distinct diabetic populations: with a small number showing bone loss from the forearm but the majority showing increased bone mass associated with increased body weight. The findings in our study are similar to Johnston (1985) who showed that bone mass is increased in postmenopausal women with Type II diabetes.

The higher bone density in diabetic subjects can be explained in several ways. Hyperinsulinaemia commonly occurs in non-insulin dependent diabetes (Smith and Hall 1973). Insulin has been shown to have a stimulatory effect on osteoblast proliferation and mitogenesis in vitro (Ernster et al 1985), and this may account for the higher bone density at the hip and spine. Sambrook et al (1988) failed to demonstrate any positive relationship between serum insulin level and bone density in normal subjects.

Alternatively, diabetic subjects may have a higher fat mass which produces a higher circulating oestrone levels than non-diabetic subjects. Oestrone has a stimulatory effect on bone and this may increase bone density. This explanation is less likely in the light of our findings, for the effect of diabetes on bone density is independent of the body mass index.

6.5.3 Body mass index

The body mass index was highly correlated with bone density at all sites and is one of the most important predictors of bone density in our study.

Women who were thin had a greater risk of hip fracture (Affram 1964, Wootton 1979, Wyshak, 1981, Hutchinson et al 1979, Paganini-Hill et al 1981, Williams et al 1982, Dalen and Olsson 1975). A thin body-build is also a risk factor for vertebral fractures in men (Seeman et al 1983).

A high body mass may be associated with a higher peak bone mass and/or a reduced rate of bone loss after menopause; both of which will result in a higher bone density in old age. Obesity may also increase the amount of biologically available oestrogen. As most oestrogen is formed from the conversion of androstenedione to oestrone in fat cells, obese women produce more oestrone than thin women (Grodin et al 1973, Schindler et al 1972, McDonald et al 1978).

6.5.4 Mental test score

Mental status was assessed by a questionnaire often used in hospitals in the United Kingdom (Hodkinson 1972, Iredale et al 1986). This questionnaire had been modified and tested on a sample of 418 healthy elderly subjects in a previous survey in Hong Kong (Woo et al 1988). Some of the questions were modified according to the local culture (refer to appendix I).

There was a significant positive association between the mental test score and bone density at the hip (after adjusting for age). The mental test score was also an important predictor of bone density at the hip. One possible explanation is that more demented subjects might have been physically less active, resulting in a faster bone loss at the hip. However, in our study, the number of hours subjects spent walking outdoors was not associated with the mental test score, and current exercise patterns were not been found to be associated with bone density. Hence the association between the mental test score cannot be due to the confounding effect of physical activity.

There is a high prevalence of dementia in patients with hip fractures, and it is generally assumed that this can be accounted for by frequent falls among demented patients. An alternative explanation for the association between the mental test score and bone density lies in the blood aluminium level. Aluminium is associated with the two hallmark neuropathological lesions of Alzheimer's disease: senile plaques (Candy et al 1986) and neurofibrillary tangles (Perl and Brody 1980). The negative calcium balance in elderly Chinese women, together with a high aluminium intake, may accelerate mental deterioration in the elderly. As a negative calcium balance may lead to osteoporosis, a low bone density was associated with a low mental score. The relationship between bone density and dementia was investigated in hip fracture patients in the United Kingdom (Wood et al , 1988). No significant difference in either mental test score or Singh Index was found between areas with a different aluminium content in the water supply. There was no correlation between bone density and dementia. In that study, the Singh Index was used to quantify bone density. This method was much less precise than X-Ray densitometry, which had enabled us to document a positive correlation between mental test score and bone density.

As poor mental function may also lead to more falls among the elderly, affected subjects will be rendered dually susceptible to hip fractures. This indicates that subjects with poor mental function are a special at-risk group for the prevention of hip fractures in the elderly.

6.5.5 History of hip fractures

In this study women who had a history of a hip fracture had a lower mental score, body mass index and bone density than other women. After adjusting for the mental score and body mass index there was no association between hip fracture and bone density. This indicated that the relationship between the bone density and hip fracture was confounded by the body mass index and the mental function of the subjects.

6.5.6 Calcium intake, physical activity and other risk factors

It has previously been found that patients with hip fractures consumed less calcium and performed less load-bearing exercise than controls (Chapter 3). The small percentage of subjects who reported regular consumption of dairy products in the past had a higher bone density at the hip. Nevertheless current calcium intake was unrelated to bone density. The variation in the calcium intake of the subjects who cooked for themselves was small. Due to the small sample size (n=31), for investigating the relationship between current calcium intake and bone density, the statistical power was small. The conclusion here seemed to be that regular dairy product consumption in the past was associated with an increased bone density, but no conclusion can be made about the relationship between current calcium intake and bone density.

Both past and current load-bearing activity patterns were unrelated to bone density. The subjects in this study were selected for they had to be capable of self-care to live in a hostel. Hence they are in general physically active. As the subjects did not differ much in exercise patterns, an association between bone density and load-bearing activities was not found. Hip fracture patients represent a comparatively less healthy sector of the population, and their exercise patterns was different from healthy controls.

Despite previous publications, nulliparity and an early menopausal age were not associated with a reduced bone density. Alcohol consumption and and smoking were relatively uncommon among Chinese women, and were not important in determining bone density. Diuretic use was not associated with bone density at the hip or spine.

6.5.7 The value of measuring bone density

The value of bone density measurements lies in its application in the prevention of fractures. Though Melton et al (1988) has proposed a bone density threshold of one g/cm^2 for hip fracture, this may not be applicable to different populations. Moreover, the risk of hip fracture are not related solely to bone density, but such factors as a tendency to fall and the ability to counteract falls may be as important.

It is also irrational to propose that women with a bone density below a certain statistically defined normal value should be treated. Perimenopausal women should have risk factors assessed and bone density measured. The decision to start oestrogen replacement should be based on these as well as its other benefits (on the cardiovascular system) and other side effects (on inducing endometrial cancer).

In older women, the value of bone density measurements may lie in assessing the progress of certain therapies (eg. calcitonin treatment) by serial measurements. Women who already have symptoms of osteoporosis e.g. severe low back pain or fracture should also have the bone density measured for decisions on therapy.

6.5.8 Prediction of bone density at the hip and spine

Stepwise multiple regression was used to find the combination of predictor variables that would account for most of the variance in bone density at the spine and hip. Age, body mass index and the mental score were significant predictors of bone density for all sites at the hip. In addition, being a diabetic was significant in predicting bone density at the intertrochanteric area and Ward's triangle. In general, the combination of these determinants account for 30-40 % of the variance in bone density at various sites in the hip. Hence there was a large part of the variance in bone density that was not accounted for.

Prediction was particularly poor for the spine. The best combination of predictors i.e. body mass index and being a diabetic, accounted for only 16% of the variance in bone density at the spine.

The conclusion seem to be that any combination of risk factors cannot be used as a replacement for measurements of bone density in order to identify subjects with a low bone density. Nevertheless, where resource are limited and measurements of bone density are expensive (as they currently are), these factors may be a guideline for screening. It seems reasonable that those who are old, frail, have a low mental score, and who already have a hip fracture are suitable candidates for bone density measurements. Therapeutic treatments can be applied to the 'at risk group', and progress of treatment can be monitored by bone density measurements.

Chapter 7

The prevention of fracture of the proximal femur in Hong Kong

7.1 Risk factors and fracture prevention

A low calcium intake and a lack of load-bearing exercise are important risk factors for fracture of the proximal femur in Hong Kong . Other risk factors include a history of falls, drinking alcohol and a history of a stroke.

The relationship between different forms of load-bearing exercise and the risk of fracture of the proximal femur has been clearly demonstrated in this study, despite previous negative findings. The advantages of physical exercise programmes in preventing fractured femur are: cheap to administer, potential good patient compliance and health benefits other than the effects on bones (Council On Scientific Affairs 1984).

The dietary intake of calcium is extremely low in Chinese. Even though the results of clinical trials on calcium supplementation in Western populations are controversial, the effects of calcium supplementation in Chinese may be much larger. Moreover, the combined effects of calcium supplementation and exercise programmes is unknown. It is important to conduct trials to measure such effects.

The patients with fracture of the proximal femur are more susceptible to falls than the controls. Falls can be prevented by simple measures in the home environment such as the removal of obstacles and the building of rails to facilitate walking for the disabled elderly. Exercise programmes also have the potential to improve co-ordination and preventive mechanisms, hence reducing both the likelihood and severity of injury after a fall.

A low vitamin D level was found to be more prevalent among fracture of the proximal femur patients than controls. Vitamin D deficiency in the elderly can be prevented by increasing the dietary intake or by increasing exposure to sunlight. The hours of exposure to sunlight had been found to be a more important determinant of blood vitamin D level than dietary intake. In Hong Kong , there is sunshine for most of the year, and an adequate exposure can be ensured by mobilizing the elderly outdoors. This can be readily accomplished by outdoor exercise programmes.

A positive relationship between current activity and calcium intake with bone density at the hip or spine has not been demonstrated. Nevertheless, the bone density of women who consumed dairy products regularly in the past was higher than women who did not. Physical activity may prevent hip fractures by mechanisms other than increasing bone density. These include the prevention of falls and the ability to counteract falls. The maintenance of an adequate calcium intake in young adulthood is important in building up and retaining normal bone density at anatomically important sites.

In elderly populations, low bone density is prevalent in frail and demented subjects. As a low bone density is the most important determinant of hip fracture, special attention should be directed to this group. The prevention of falls, the maintenance of activity and an adequate dietary intake to prevent further loss in body weight and bone density may be particularly important in these subjects.

7.2 Existing policy on health and welfare of the elderly

In 1987, 7.6% of the population in Hong Kong was older than 65 years. The mean life expectancy was 72 years for men and 78 years for women (Hong Kong Census and Statistics Departmen 1987).

The aging of the population has been appreciated by the Hong Kong Government, and plans were made in 1977 to expand services for the elderly on a broad scale, with the objective of promoting the well-being of the elderly through care in the community and by the community (Government White Paper 1977).

In 1987, community support services and residential services for the elderly included home-help services, multi-service centres, day care centres and social centres, homes and special accommodation for the elderly (Director of Social Welfare 1987).

Special health services for the elderly are provided only in the form of 434 geriatrics beds distributed in various government and subvented institutions, and 120 geriatric day-hospital beds (Director of Medical and Health Department 1987). There is no programme directed towards health maintenance in the elderly. Moreover, the outpatient services provided by government clinics are directed at episodic care and cure. There is no primary health care system which can provide continuous and comprehensive health care to the elderly or to other sectors of the population.

Health education is organized by the Central Health Education Unit of the Medical and Health Department (Director of Medical and Health Department 1987). The unit has the task of educating a large number of 'at-risk' groups with limited resources. In 1986-1987 the elderly was not a target group for special health education programmes.

7.3 Health programmes for the prevention of fracture of the proximal femur

The exact relative risk and the mechanisms by which the risk factors operate need to be documented by follow-up studies. Nevertheless, in view of the large population at risk and the magnitude of the problem, preventive programmes should not be delayed.

Walking exercise and oral calcium supplements are important components of such preventive programmes, which should ideally be administered by multidisciplinary teams with doctors, dietitians, physiotherapists and social workers. The home environment should also be screened for potential hazards, with advice on accident prevention. Special attention should be paid to frail and demented elderly subjects for they may have a reduced bone density and are at a high risk of proximal femur fractures.

Primary health care is under extensive review in Hong Kong. It is obvious that the elderly are one of the groups which would benefit most from basic preventive and rehabilitative programmes. The objectives of primary health care in the elderly should be to maintain the well-being of the elderly by community care rather than institutionalized care. Efforts should be directed at preventing such debilitating conditions as fracture of the proximal femur in the elderly.

Chapter 8

Conclusions

8.1 Incidence of fracture of the proximal femur in Hong Kong

Fracture of the proximal femur is an important public health problem in Hong Kong. The incidence among elderly men increased from 320 per 100,000 to 1156 per 100,000 population, and the incidence among elderly women increased from 716 per 100,000 to 1521 per 100,000 population.

The mean length of hospital stay was 12 days in Queen Elizabeth Hospital (with rehabilitation in Kowloon hospital), and 26 days in Kwong Wah Hospital. As the general population ages, the magnitude of the problem will continue to increase.

8.2 Risk factors for fracture of the proximal femur in Hong Kong

A case-control study has been conducted in 1200 subjects, and some insight has been gained into the risk factors for fracture of the proximal femur in Chinese.

Regular load-bearing exercise is protective for fracture of the proximal femur. The risk of not walking every day was significantly higher than one. The calcium intake of Chinese subjects were much lower that of Caucasians, and the major source of calcium in the Chinese diet was from green vegetables. Patients with fracture of the proximal femur consumed significantly less calcium than controls, and the risk of fracture increased with a low calcium intake.

More patients with fracture of the proximal femur patients who were younger than 70 years reported falls in the previous year than controls. The relative risk for drinking alcohol every day was four. A history of a stroke was also a significant risk factor.

There was few confounding effects between the various risk factors. The attributable risk was highest for a lack of load-bearing activity and a low calcium intake. About 13% of the risk of fracture of the proximal femur was attributable to the lowest quintile of load-bearing activity, and 19% was attributable to the lowest quintile of calcium intake.

8.3 Vitamin D and fracture of the proximal femur in Hong Kong

The serum vitamin D level amongst the elderly was higher in Hong Kong than temperate countries. The normal 95% confidence limits were 14.6-51.3 μg/L for men and

13.7-40.3 μg/L for women. Nevertheless, The blood 25-hydoxyvitamin D level was significantly lower in 200 fracture of the proximal femur patients than 317 subjects in the same age groups. Twenty of the male patients and 30% of the female patients had a 25-hydroxyvitamin D level below the 95% confidence limit of the controls.

There was no difference in serum calcium and alkaline phosphatase levels between patients and controls. The low vitamin D levels in fracture of the proximal femur patients was not accompanied by blood biochemistry diagnostic of frank osteomalacia.

Fracture of the proximal femur patients with a low vitamin D level were exposed to less outdoor activities than patients with a normal level. This again highlights the benefits of outdoor exercise programmes for the elderly .

8.4 Determinants of bone density in the elderly

Age, body mass index and mental test score are the important determinants of bone density in the elderly. Regular dairy products consumption in young adulthood contributed to a higher bone density in the elderly. Frail and demented subjects are at special risk of hip fracture for they are also susceptible to falls.

8.5 Prevention of fracture of the proximal femur in Hong Kong

The maintenance of a high calcium intake and regular load-bearing activity are important public health measures for the prevention of fracture of the proximal femur in Hong Kong. Special attention should be directed to frail and demented subjects who are at particularly high risk. The effects of preventive programmes should be evaluated by randomized controlled clinical trials.

In view of the large elderly population in Hong Kong, and the limited community resources, special preventive programmes are not immediately feasible. A practical alternative is to educate all gerontological workers, so that they can implement preventive measures as part of their work with the elderly. Preventive and rehabilitative programmes for the elderly are an essential element of the future primary health care system in Hong Kong.

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Appendix I:

Questionnaires

Case-control study on fracture of the proximal femur
in Hong Kong Chinese

Date of interview: ______________________

1. Name of subject: ______________________

2. Serial number: ______________________

3. Hospital number: ______________________ Bed no.: __________

4. X-Ray number: ______________________

5. Date of admission: ______________________

6. Type of fracture:
   1. cervical
   2. intertrochanteric

7. Side of fracture:
   1. right
   2. left

8. Operation done: ______________________ Date: ______________

9. Address: ____

   District code:

10. Sex:
    1. male
    2. female

11. Date of birth: ______________________ Age: ______

12. Marital status:
    1. single
    2. married
    3. widowed
    4. divorced or separated

13. Place of origin:
    1. Guangdong
    2. other parts of China
    3. other countries
    4. Hong Kong

14. Years lived in Hong Kong:
    1. less than 10 years
    2. 10-19
    3. 20-29
    4. 30-39
    5. 40-49
    6. 50-59
    7. 60-69
    8. 70+

15. Accommodation: 1. private housing/government low cost purchasing scheme
2. government estates
3. temporary housing area
4. squatter/hut/stone house
5. private old folks home
6. government/v.a. old folks home
7. institute
8. hospital
9. hostel/bed

16. Do you live with: 1. relatives
2. other people
3. alone for ________ years

17. Floor: __________

18. Lift: 1. Yes 2. No

19. Do you usually: 1. walk 2. take lift 9. no need

20. How many times do you walk up per day: ________
(20 steps per floor)

21. Did the fall happen 1. work place
2. inside home
3. outside home but in housing block
4. market
5. street
6. elsewhere

22. Time of day when it occurred ________ hr (24 hr. clock)

23. How did it happen 1. fall from walking on the level
2. fall from standing or sitting
3. fall on slope
4. fall while running
5. traffic accident
6. fall from stairs/height

24. Describe the Incident of the Fall

____

____

25. Before you had the fall, were you able to:

0. go out of home, up and downstairs without support and aid
1. go out of home, up and downstairs with walking aid
2. go out of home, up and downstairs with support
3. go out of home, on the level with walking aid
4. go out of home, on the level with human support
5. walk around in house without support
6. walk around in house with stick/walking aid
7. walk around in house with support onto furniture etc.
8. walk around in house with human support
9. bed-ridden

26. Before you had the fracture, did you:
1. everyday
2. on alternate days
3. once-twice weekly
4. occasionally
5. never

a. walk to the shops/on the street
b. walk upstairs
c. walk uphill]
d. carry a load while walking
e. housework (washing clothes, cleaning)

27. When you were 30-35 years old, did you:
1. everyday
2. on alternate days
3. once-twice weekly
4. occasionally
5. never

a. walk up and down hill/slope
b. carry a load while walking (water, basket, carry a baby, etc)
c. do heavy housework (wash clothes, clean floor)

28. Have you fallen in past 1 year? 1. Yes 2. No

a. need to be treated by a doctor ______ times

b. need to be treated by a Chinese osteopath ______ times

c. no treatment needed ______ times

29. Have you broken any bones in the preceding 5 years? 1. Yes 2. No

a. femur ______ times

b. vertebrae ______ times

c. forearm bone ______ times

e. others ______ times

30. Smoking status.
1. current smoker
2. ex-smoker
3. never smoked (proceed to Q.32)

31. When you first smoked, you smoked ______ /day

for ______ years

a. if changed, then you smoked ______ /day

for ______ years

b. if ex-smoker, stopped smoking ______ years ago.

32. Do you take alcoholic drink regularly?
1. everyday
2. on alternate days
3. once-twice weekly
4. occasionally
5. never
6. ex-drinker

33. Were you ever hospitalized because of a drinking problem? 1. Yes 2. No

If yes, reason for admissions: ______________________

34. Have you had:

a.	heart disease	1. Yes	2. No
b.	hypertension	1. Yes	2. No
c.	C.V.A.	1. Yes	2. No
d.	diabetes	1. Yes	2. No
e.	thyroid disease	1. Yes	2. No
f.	renal disease	1. Yes	2. No

35. In the month before you had the fracture, were you taking:

a.	drugs for heart disease	1. Yes	2. No
b.	drugs for hypertension	1. Yes	2. No
c.	sedation drugs	1. Yes	2. No

36. Age at menarche:

37. How many pregnancies:

38. How many live births (born after 28 weeks gestation):

39. Number of children breast-fed:

40. Age at menopause:

41. Any drugs given for menopause? 1. Yes 2. No 3. Don't know

42. Did you have your ovaries removed? 1. Yes 2. No 3. Don't know

reason for operation: ______________________

43. Are you working at present? 1. Yes 2. No

44. What is your occupation? ______________________

45. What was your occupation at 30-35 years old? ______________

46. What was your occupation at menopause? ______________

47. How many time in a week do you eat the following food:-

1. everyday
2. on alternate days
3. once-twice weekly
4. occasionally
5. never

a. milk
b. milk drinks (cocoa, ovaltine, holick)
c. milk in tea/coffee
d. cheese
e. bread/cake/biscuit
f. soya bean curd
g. vitasoy
h. small fish
i. green vegetable
j. calcium tablets
k. vitamins tablet

Questionnaire for cross-sectional survey of bone density in the elderly

1) HKID Number

2) Serial Number

3) Date of birth (as in ID card)

4) Are you on drugs for these diseases? *[yes = 1, no = 2]*
   a) diabetes mellitus
   b) thyroid disease
   c) diuretics

5) When did you have your menarche (age)?

6) How many children did you gave birth to ?

7) Did you have your ovaries removed?

8) When (age)?

9) Were you given any 'special drugs' after your ovaries were removed?

10) When did you have your menopause (age)?

11) Do you smoke? *[Current = 3, ex = 2, never = 1]*

12) If 3 and 2, for how many years?

13) If 3 and 2, how many a day?

14) Do you drink? *[Current = 3, ex = 2, never = 1]*

15) If 3 and 2, for how many years?

16) How many days a week?

17) Have you ever fractured your
   a) forearm
   b) spine
   c) hip

Physical activity

18) What was your main occupation?

19) When you were 30 years old, how many days in a week did you

a) walk uphill?

b) carry a heavy load while walking?

c) work actively while standing?

d) play ball-games?

20) In the last week how many hours did you spend in

a) walking outdoors?

b) exercise while standing?

Calcium intake

21) When you were 30 years old, how often did you consume the following food-items?
[never = 0, occasional = 1, often = 2]

d) milk and cheese?

b) green vegetables and soya products

c) fish and seafood

22) Do you eat the food provided by the hostel or cook for yourself?
[hostel food = 1, cook yourself = 2]

Food diary day 1

Breakfast

Lunch

Afternoon tea

Dinner

Snack

Food diary day 2

Breakfast

Lunch

Afternoon tea

Dinner

Snack

Food diary day 3

Breakfast

Lunch

Afternoon tea

Dinner

Snack

Appendix II

Publications related to the thesis

Physical activity and calcium intake in fracture of the proximal femur in Hong Kong

E Lau, S Donnan, D J P Barker, C Cooper

Abstract

In Hong Kong physical activity and calcium intake of 400 Chinese men and women with hip fractures were compared with those of 800 controls. Daily walking outdoors, upstairs, uphill, or with a load protected against fracture. This was independent of cigarette smoking and alcohol consumption. Higher levels of reported activity in middle life were also protective. Average calcium intake was around one quarter that in Britain because of the low consumption of dairy products. Differences in calcium intake depended mainly on consumption of green vegetables and small fish. High intake protected against hip fracture.

These findings point to the importance of maintaining daily physical activity and calcium intake in urbanised Chinese populations.

Introduction

Hip fractures are an increasing public health problem among elderly Chinese in Hong Kong.[1,2] This population eats a traditional Chinese diet, which is low in calcium, and urbanisation has reduced their physical activity. The contribution of these two factors to the rising incidence of fracture is unknown. We compared calcium intake and activity in elderly Chinese men and women with hip fractures and controls of similar ages.

Patients and methods

The study group comprised 400 patients with radiologically diagnosed hip fracture who were admitted consecutively to the orthopaedic wards of two main hospitals in Kowloon. Their activity and diet were compared with those of two sets of controls. Hospital controls comprised surgical inpatients from the wards of the same hospital. No diagnostic groups were excluded, and the first patient admitted after the case of the same sex and within five years of age was recruited. Community controls came from two sources. For patients aged over 70 they were systematically sampled from a register for the old age allowance in Shatin; for patients aged under 70 controls were randomly selected from attenders at the Chinese University general practice unit in Shatin. Community controls were individually matched to the patients by sex and five year age group. When a control refused to participate a substitute was selected.

All patients in the study group and controls were interviewed by one of two trained interviewers with a structured questionnaire. They were asked about their history of falling, cigarette smoking, and alcohol consumption. The usual frequency of carrying out various forms of weight bearing physical activity was assessed by inquiring about the frequency of walking outdoors, upstairs, uphill, and with a load during the six weeks before admission to hospital. The frequencies of walking uphill and with a load at around the age of 35 were used as indices of past physical activity. Current calcium intake was assessed from the weekly frequency of consumption of nine foods that contain calcium and are commonly eaten in the Chinese diet. The intake was calculated from the calcium content of each food,[3] typical portion sizes, and the frequency of consumption in a week. The results tended to underestimate the total intake.

The data were analysed with a conditional multiple logistic regression for matched case-control studies. As the estimates of relative risk when patients in the study group were compared with community controls were similar to those obtained when they were compared with hospital controls the two control groups were amalgamated.

Results

Eighteen patients could not be interviewed because of their poor mental state, and additional patients were recruited to make up 400. The rate of response among the controls was 90%. Table I shows the age and sex distribution of the patients in the study group. There were more older women, and the totals were 280 women and 120 men. Significant increases in the risk of hip fracture were found in people who were current or previous cigarette smokers (relative risk=1·3, 95% confidence interval 1·0 to 1·7), who consumed alcohol daily (3·9, 2·3 to 6·7), and who had reported a fall within the previous year (1·8, 1·3 to 2·5).

Table II shows the relation between current physical activity and the relative risk of hip fracture. Among women the risk was up to 2·1 times greater in those who reported walking outdoors, upstairs, uphill, or with a load less than once a day. After adjustment for cigarette smoking and alcohol consumption the

TABLE I—*Age and sex distribution of patients with hip fracture*

Age (years)	Women	Men
<70	54	47
70-79	108	45
≥80	118	28
Total	280	120

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…II—*Current physical activity and risk of hip fracture in 400 patients with hip fracture and 800 controls**

…ency of activity	Women: No of patients	Women: No of controls	Women: Relative risk: Non-adjusted	Women: Relative risk: Adjusted†	Women: Relative risk: 95% Confidence interval	Men: No of patients	Men: No of controls	Men: Relative risk: Non-adjusted	Men: Relative risk: Adjusted†	Men: Relative risk: 95% Confidence interval
…ing outdoors:										
…s than once a day	105	131	1·7	1·7	1·2 to 2·3	25	40	1·3	1·3	0·7 to 2·4
…ce daily or more	175	409	1·0	1·0		95	200	1·0	1·0	
…ing upstairs:										
…than once a day	137	323	1·4	1·4	1·0 to 1·9	71	133	1·2	1·0	0·6 to 1·7
…ce daily or more	97	235	1·0	1·0		49	107	1·0	1·0	
…ing uphill:										
…s than once a day	267	523	1·5	1·6	0·8 to 3·1	111	216	1·4	1·9	0·7 to 4·7
…ce daily or more	13	37	1·0	1·0		9	24	1·0	1·0	
…ing with a load:										
…s than once a day	268	513	2·1	2·3	1·2 to 4·7	111	218	1·3	1·4	0·6 to 3·3
…ce daily or more	11	45	1·0	1·0		9	22	1·0	1·0	

…ormation was not available for all subjects.
…justed for cigarette smoking and alcohol consumption.

…LE III—*Past physical activity and risk of hip fracture in 400 patients with hip fracture and 800 controls**

…quency of activity	No of patients	No of controls	Relative risk: Non-adjusted	Relative risk: 95% Confidence interval	Relative risk: Adjusted†	Relative risk: 95% Confidence interval
Women						
…lking uphill:						
Less than once a day	53	154	1·6	1·1 to 2·2	1·5	1·1 to 2·3
Once daily or more	227	406	1·0		1·0	
…lking with a load:						
Less than once a day	126	272	1·2	0·9 to 1·5	1·2	0·9 to 1·6
Once daily or more	153	286	1·0		1·0	
Men						
…alking uphill:						
Less than once a day	19	51	1·5	0·8 to 2·8	1·5	0·8 to 2·9
Once daily or more	101	189	1·0		1·0	
…alking with a load:						
Less than once a day	38	103	1·6	1·0 to 2·6	1·7	1·1 to 2·8
Once daily or more	82	137	1·0		1·0	

Information was not available for all subjects.
Adjusted for cigarette smoking and alcohol consumption.

…ABLE IV—*Dietary calcium intake and risk of hip fracture in 400 patients with hip fracture and 800 controls*

Fifths of the distribution of calcium intake (mg/day)	No of patients	No of controls	Relative risk: Non-adjusted	Relative risk: 95% Confidence interval	Relative risk: Adjusted†	Relative risk: 95% Confidence interval
Women						
<75	93	137	1·9	1·2 to 2·9	1·9	1·2 to 2·9
75–	47	72	1·8	1·1 to 3·0	1·9	1·1 to 3·1
83–	42	105	1·1	0·7 to 1·9	1·1	0·7 to 1·9
129–	57	126	1·3	0·8 to 2·0	1·2	0·8 to 2·0
≥244	41	120	1·0		1·0	
Men						
<75	44	67	2·0	1·1 to 3·7	2·1	1·1 to 4·2
75–	14	30	1·4	0·6 to 3·2	1·4	0·6 to 3·4
83–	23	44	1·6	0·8 to 3·2	1·7	0·8 to 3·7
129–	20	40	1·5	0·7 to 3·2	1·5	0·7 to 3·2
≥244	19	59	1·0		1·0	

†Adjusted for cigarette smoking and alcohol consumption.

increased risks associated with all these activities remained significant ($p=0·05$) except for that associated with walking uphill. Among men, after adjustment, increased risks were associated with walking outdoors, uphill, or with a load less than once a day. These were not significant.

Table III shows the relation between past physical activity and the relative risk of fracture. Among women a significant increase in risk associated with walking uphill less often than once a day remained after adjustment for smoking and alcohol ($p<0·05$). For men a significant increase in risk associated with walking with a load less than once a day also remained after adjustment ($p<0·05$).

The mean daily calcium intake of the patients in the study group was lower than that of the controls. The intake was 128 mg in female patients (interquartile range 75-176 mg) compared with 168 mg in female controls (76-214 mg) and 141 mg in male patients (75-164 mg) compared with 177 mg in male controls (75-226 mg). Table IV shows a fall in relative risk of hip fracture with increasing calcium intake in women and men. This trend remained significant after adjustment for cigarette smoking and alcohol intake in women ($\chi^2=21·4$, df=1, $p<0·01$) and men ($\chi^2=4·4$, df=1, $p=0·036$). In the logistic regression the trends in risk with physical activity and calcium intake were independent of each other.

Discussion

We showed that among elderly women in Hong Kong regular daily weight bearing activity and a higher dietary calcium intake were associated with a reduced risk of hip fracture. Among elderly men there was a similarly strong relation with calcium intake but the relation with activity was not significant.

The rates of response for both patients and controls were high. There were, nevertheless, potential sources of bias in both sets of controls. The hospital control group may have overrepresented people with an inactive lifestyle and atypical diet, whereas the community control group may have been biased towards fitter individuals who had moved out of Kowloon to a newly built suburb. The differences in physical activity and calcium intake between patients and controls were, however, similar for both control groups.

In 1970 Chalmers and Ho suggested that hard physical labour might be the factor that protected the Bantu, the Singaporean, and the Hong Kong Chinese against hip fracture.[4] The increasing incidence of hip fracture that has been shown in the Chinese population of Hong Kong could be the result of rapid urbanisation and a reduction in weight bearing physical activity.[12]

The mean daily intake of calcium was low in both patients and controls in comparison with Britain. The estimated daily intake among controls was 171 mg compared with 689 mg in a population of similar age in Southampton (see accompanying paper, p 1443). There was little overlap in the two distributions. Calcium intake in Hong Kong was assessed from only nine food items and will have been underestimated. This, however, is unlikely to account for the large difference from Britain. Low calcium intake is a known characteristic of the Chinese diet,[2] in which consumption of dairy products is low. Rice is eaten with one or two other dishes in every meal in the traditional Chinese diet. These dishes can be of mixed (such as meat fried with green vegetables) or single ingredients (such as steamed fish); 78% of patients and 81% of controls ate green vegetables daily; 17% of patients and 27% of controls reported that they ate small fish at least once a week. Soya bean curd, which is an important potential source of calcium in the Chinese diet, was eaten at least once a week by 35% of controls but by only 27% of patients. In contrast to the data from Southampton, calcium was found to protect against fracture in both women and men. In the past low calcium intake might have been offset by a high level of weight bearing physical activity, which maintained bone mass. The decline in activity which followed the construction of high rise apartments and the disappearance of walking space may have unmasked the adverse skeletal effect of a low calcium intake.

Public health strategies to reduce the rising incidence of hip fractures in urbanising oriental populations are urgently required. Our results point to the importance of maintaining physical activity and calcium intake in elderly Chinese people who grew up in rural communities, characterised by high levels of physical activity and a diet low in calcium, but are now mostly living in flats in high rise buildings while continuing to eat a traditional diet.

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Plasma 25-Hydroxyvitamin D Concentration in Patients with Hip Fracture in Hong Kong

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Abstract. The serum concentration of 25-hydroxyvitamin D level and plasma albumin-adjusted calcium, phosphate, and alkaline phosphatase levels were studied in 200 patients with hip fracture (age range 49–93 years) and 427 elderly subjects living in the community (age range 60–90 years). The mean serum 25-hydroxyvitamin D levels in controls were higher than in temperate countries, but the 25-hydroxyvitamin D concentration was significantly lower in the patients than the controls for all sex and age groups. There was little difference in albumin-adjusted calcium and alkaline phosphatase levels, but the phosphate level was higher in the patients than in the controls. None of the patients with a low 25-hydroxyvitamin D level had a blood picture suggestive of osteopathy resulting from vitamin D deficiency or frank osteomalacia. Hip fracture patients with a low 25-hydroxyvitamin D level were much less ambulant and went outdoors much less frequently than hip fracture patients with a normal vitamin D level. A low vitamin D level was a risk factor for hip fracture in Hong Kong Chinese, and may be prevented by frequent outdoor exposure.

The incidence of hip fractures in Hong Kong has increased in the last 20 years to a rate of about 10/1,000 in subjects 70 years and above [Lau, 1988].

A low vitamin D level has been found in fractured proximal femur patients living in a temperate climate. Ulivieri et al [1986] compared fractured femoral neck patients with fractured vertebral patients, and found that both the serum 25-hydroxycholecalciferol and the urinary calcium were lower in patients with fractured proximal femur. This confirmed earlier findings by Lips et al. [1982], Hoikka et al. [1982], Baker et al. [1979], and Baylink et al. [1977]. In these studies the vitamin D levels of fractured proximal femur patients were compared to population controls in Europe and North

America. The vitamin D status of hip fracture patients had not been studied in Asian populations.

It is well known that severe and prolonged vitamin D deficiency can cause osteomalacia. It has also been suggested that subclinical vitamin D deficiency may play a role in the pathogenesis of osteoporosis [Parfitt et al., 1982], which is a major public health problem in the elderly throughout the world.

Subjects and Methods

200 hip fracture patients (age range 49–93 years) admitted consecutively to the orthopaedic wards of Queen Elizabeth Hospital of Hong Kong were studied. All diagnoses were confirmed by X-ray and operative findings, and no eligible patients were excluded in the period of the study, which was from February to November in 1 year. A blood sample was taken on the day of admission, with the subjects in a non-fasting state.

The control subjects were 427 residents in sheltered housing (age range 60–90 years). They were participants in a survey of the elderly conducted from June to November in 1 year. Blood was taken without fasting.

Serum calcium, phosphate, alkaline phosphatase and albumin levels were measured by standardized techniques on an American Monitor Parallel Analyzer (American Monitor, USA). The albumin adjusted calcium levels were derived by the following formula [Payne et al., 1973]: albumin-adjusted calcium concentration = measured calcium concentration + 0.025 (40-albumin concentration).

An aliquot of plasma was stored at −70 °C for assay of 25-hydroxyvitamin D (25-OHD), by competitive protein-binding assay as previously described [MacDonald and Swaminathan, 1988]. Serum was mixed with acetonitrile and centrifuged. The supernatant was applied to a Sep Pak C18 cartridge (Waters Associates, USA), which had been prepared by washing with acetonitrile and water. The cartridge was then washed with water and methanol. The 25-OHD was then eluted with acetonitrile and dried under nitrogen. The extract was stored under nitrogen at −20 °C until assay, which was done within 2 days. Recovery of extraction was monitored for each specimen by adding a small amount of labelled 25-OHD to the sample and this ranged from 60 to 80%.

The extracts were reconstituted in ethanol and assayed by a competitive protein binding method using plasma from a vitamin D-deficient pig at a dilution of 1 in 4,000. All values were individually corrected for losses throughout the whole procedure. The interassay coefficient of variation was 6.9%.

The mean serum 25-OHD level was compared with values from various temperate countries as quoted by McKenna et al. [1985]. The 25-OHD levels were converted from nanomoles per litre to micrograms per litre by multiplying by a factor of 0.4 [Bouillon et al., 1987].

The normal ranges for the plasma 25-OHD, albumin-adjusted calcium, phosphate and alkaline phosphatase were the 95% confidence limits (mean ± 1.96 standard deviation) of the controls. The unpaired t test was used for comparing means and proportions between patients and controls.

Results

Table 1 shows the mean 25-OHD level according to age and sex. In all groups, the levels were lower in the hip fracture patients than the controls ($p < 0.01$ by the t test). Moreover, among patients, the 25-OHD level was lower in women than in men ($p < 0.01$ by the t test). There was no statistically significant difference in 25-OHD concentration between patients in different age groups.

20% of the male patients and 30% of the female patients had a 25-OHD level below the 95% confidence limit of the controls. The normal 95% confidence limits were 14.6–51.3 μg/l for men and 13.7–40.3 μg/l for women. Most of the patients with abnormal 25-OHD levels were very old, 78% of men and 68% of women were 80 years and over. The mean 25-OHD level in the con-

Table 1. 25-OHD levels in patients and controls

	Plasma 25-OHD	
	patients	controls
Men younger than70	22.5 ± 7.2 (28)	33.9 ± 10.2 (63)
Men 70 years and over	18.5 ± 6.9 (32)	32.2 ± 8.6 (90)
Women younger than 70	17.8 ± 5.5 (31)	29.0 ± 6.2 (81)
Women 70 years and over	17.1 ± 6.2 (107)	26.0 ± 6.8 (134)

Values are mean ± SD with the number of subjects given in parentheses. The vitamin D level was lower in patients than controls at the 0.001 level for all groups.

Table 2. Serum 25-OHD levels in temperate countries, Australia and Hong Kong

Author	Year	Country	Mean 25-OHD level, µg/l
Von Knorring et al.	1982	Finland	6.8
Schmidt-Gayk et al.	1977	FRG	8.4
McKenna et al.	1985	Ireland	8.4
Lester et al.	1977	UK	8.6
Rapin et al.	1982	Switzerland	> 9.2
Chapuy et al.	1983	France	11.9
Omdahl et al.	1982	USA	12.4
Lund et al.	1975	Denmark	22.0
Tassie et al.	1985	Australia	27.2
Present study		Hong Kong	27.0

The values for temperate countries were quoted by McKenna et al. [1985]. Original values presented as nmol/l were converted to µg/l after multiplying by a factor of 0.4.

trols was higher than levels from healthy old people living in the temperate zone, but was similar to the level found in Australia (table 2).

Table 3 shows the serum calcium concentration (albumin-adjusted), phosphate and alkaline phosphatase concentrations in patients and controls. There was no statistically significant difference in serum calcium (albumin-adjusted) and alkaline phosphatase levels between patients and controls, but the serum phosphate level was higher in patients than controls ($p < 0.01$ by t test).

Among patients with a low 25-OHD, none had a biochemical picture suggestive of osteomalacia. Only 1 man and 2 women had an elevated serum alkaline phosphatase level (the upper limit was 157 IU/l for men and 180 IU/l for women). None of the subjects with a low vitamin D level had an albumin-

Table 3. Serum calcium, phosphate and alkaline phosphatase concentrations in hip fracture patients and controls

Serum concentrations	Men		Women	
	patients	controls	patients	controls
Calcium, mmol/l	2.29 ± 0.13	2.28 ± 0.11	2.31 ± 0.12	2.29 ± 0.12
Phosphate level, mmol/l	1.01 ± 0.24	0.84 ± 0.17	1.10 ± 0.19	0.97 ± 0.15
Alkaline phosphatase, IU/l	107.3 ± 45.3	113.5 ± 26.7	105.4 ± 37.5	113.3 ± 33.8

Values are mean ± SD.

adjusted calcium and serum phosphate levels outside the normal ranges (the normal range for albumin-adjusted calcium was 2.06–2.50 and 2.05–2.53 mmol/l for men and women, respectively; the normal range for phosphate was 0.5–1.13 and 0.67–1.34 mmol/l for men and women, respectively.

Hip facture patients with low 25-OHD concentration were less mobile than hip fracture patients with a normal concentration. 33% of patients with a low level reported that they could walk outdoors without any aid and 30% admitted that they never walk outdoors, while 61% of patients with a normal 25-OHD could walk outdoors without any aid and only 8% said they never walk outdoors. These proportions were statistically significant at the 0.01% level by the t test.

Discussion

The 25-OHD level for both patients and controls was measured in the same laboratory and by the same technician, and the difference in 25-OHD level was unlikely to be due to interlaboratory or interobserver variation. The winter of Hong Kong is mild and lasts from December to February, with an average temperature of about 17 °C and sunshine on most days. Although we had shown a small seasonal variation in vitamin D levels [MacDonald and Swaminathan, 1988], the difference observed here is much larger and the study season was similar for both groups. A genuine difference between patients and controls was likely.

The 25-OHD level in control subjects indicated a good vitamin D nutrition status when comparison was made with populations living in a temperature climate (table 2). The latitude range for these temperate countries was 35–60° while Hong Kong lies 22.5° north of the equator. Much of the geographical difference in vitamin D level was probably due to a difference in the intensity of solar radiation. The lower 25-OHD levels in the hip fracture patients than local controls demonstrated in this study are in accordance with other studies conducted in Europe [Lips et al., 1982; Hoikka et al., 1982; Ulivieri et al., 1986]. Though the vitamin D nutrition status is good in the general population, a low vitamin D level seemed to be a risk factor for hip fracture.

There was no biochemical evidence to suggest that the hip fracture patients were vitamin D-deficient. In hip fracture patients with a low vitamin D level, there was no biochemical evidence of hypovitaminosis D osteopathy (i.e. a high serum alkaline phosphatase level accompanied by abnormal serum calcium and phosphate levels). Contrarily to prediction, the mean serum phosphate level was not low. The low phosphate level in the control group had been commented on in a previous publication [Woo et al., 1989]. The phosphate level in the hip fracture patients were in fact very close to the laboratory normal values for subjects 60 years and above (the mean was 1.01 mmol/l and SD was 0.15 mmol/l for men, and the mean was 1.13 mmol/l and SD was 0.13 mmol/l for women). The fact that none of the patients with a low 25-OHD level had frank osteomalacia (as diagnosed by blood biochemistry only) is in accordance with the studies by Uliveri et al. [1986] and Lips et al. [1982]. These authors also failed to demonstrate any difference in serum calcium, phosphate and alkaline phosphatase level between patients and controls. Hoikka et al. [1982] were the only authors who had shown a difference in serum calcium and alkaline phosphatase levels between patients and controls.

Nevertheless, osteomalacia could not be excluded with certainty here, for the use of biochemical criteria to diagnose osteomalacia is of doubtful validity. It has been demonstrated that biochemical values may be normal in osteomalacia [Anderson et al., 1966; Jenkins et al., 1973; Daw et al., 1979; Eid, 1978], and a diagnosis of osteomalacia should be made by histology.

There are other mechanisms whereby a low vitamin D level may lead to hip fracture without producing frank osteomalacia. Mild vitamin D deficiency has been shown to lead to bone resorption and osteoporosis [Baylink et al., 1977]. Vitamin D deficiency may cause muscle weakness and a proneness to falls, which is an important risk factor for hip fracture [Melton and Riggs, 1985]. Finally, the blood vitamin D level may not be a direct antecedent of hip fracture, but may be a nonspecific marker of physical inactivity and poor nutrition, which can contribute to hip fracture.

The main sources of vitamin D in human subjects are dietary intake and skin synthesis. In the elderly, plasma 25-hydroxycholecalciferol level correlates more strongly with sun exposure than with dietary vitamin D intake [Hodkinson et al., 1973; Lips et al., 1987]. In this study, hip fracture patients with a low vitamin D level were found to be less ambulant and they went outdoors less frequently than controls. Though there is adequate sunlight outdoors, an inclination to stay indoors seemed to have precluded an adequate exposure in many of the patients with hip fracture.

Most vitamin D-rich foods such as fatty fish, eggs and chicken liver are seldom consumed by elderly Chinese, whose diet is composed mainly of vegetables, lean meat and rice [Ho et al., 1988]. However, a change in dietary habits would be difficult to implement in elderly Chinese. The vitamin D nutrition status in the control group who were elderly subjects living in the community was good, and it has been previously demonstrated that regular weight-bearing exercise protects against hip fractures [Lau, 1988]. Hence, exercise programmes which mobilize subjects outdoors may maintain vitamin D level, increase bone mass and prevent hip fractures in the elderly.

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Falls and Hip Fracture in Hong Kong Chinese

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The risk factors for hip fracture were studied in four hundred patients and eight hundred community and hospital controls. Falling was found to be important as a direct cause of fracture. A history of falls was a significant risk factor for hip fracture in men and women younger than 70, but was less important in older men and women. Medical conditions and treatments did not occur more frequently in hip fracture patients with a history of falls than in patients without, and the patients with a history of falls was not less ambulant than patients without. Regular weight-bearing exercise programmes are recommended as a practical preventive measure for falls and hip fractures.

Introduction

The incidence of hip fracture in Hong Kong Chinese increased three fold in the last twenty years to reach 10 per 1000 in men and women who are seventy years and over.[1] Research in western countries showed that the high incidence of hip fracture can be attributed to two problems affecting the elderly: osteoporosis and the tendency to fall.[2] Lack of load-bearing exercise and a low calcium intake have been shown to be important risk factors for hip fracture in Hong Kong.[3] The role of falls is presented here.

Methods

Four-hundred patients with radiologically diagnosed hip fracture admitted consecutively to the orthopaedic wards of two major hospitals in Kowloon were studied. Patients with pathological fractures or who were unconscious or demented were excluded. Hospital controls were surgical in-patients from the same hospitals. No diagnostic groups were excluded and the first patient admitted after the case, of the same sex and within five years of age, was recruited. Community controls came from two sources. For patients older than 70 years, controls were systematically sampled from a register for the Old Age Allowance in Shatin; for patients younger than 70 years, controls were randomly selected from attenders at the Chinese University General Practice Unit in Shatin. Community controls were individually matched to the patients by sex and five year age group.

All subjects were interviewed by one of two trained interviewers using a structured questionnaire. Mental status was tested by orientation in time, place and person. The subjects were also asked to recall their name, age and address. Only subjects who gave correct answers to these questions entered the study. Eligible subjects were questioned on the direct cause of the fracture, a history of falls in the preceding year, a history of fracture in the last 5 years, medical history, drug history, smoking and drinking history. The frequency in a week before the fracture in which five forms of load-bearing walking activities were performed was recorded. Dietary calcium intake was also assessed by recall.

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The odds ratio and 95% confidence interval for matched pairs were calculated by conditional logistic regression, using hospital and community controls separately and then amalgamating them. The adjusted odds ratio and 95% confidence intervals were similarly calculated using the package PECAN.

Results

Eighteen patients did not pass the mental test and additional patients were recruited to make up 400. The age and sex distribution is shown in Table I. The reported cause of fracture is shown in Table II. It can be seen that 51% of the fracture resulted from falling while walking on the level.

The odds ratio for a history of falls in the preceding year was 1.9 (95% C.I. = 1.2–2.9) compared with hospital controls and 1.8 (95% C.I. = 1.2–2.7) compared with community controls. Matching both controls to a case, the odds ratio was 1.8 (95% C.I. = 1.2 = 2.6) and 2.0 (95% C.I. = 0.9–4.2) for men and women respectively. The odds ratio was much higher in subjects younger than 70 years than the other two age groups (Table III).

The odds ratio for a history of falls in the preceding year was 1.8 (95% C.I. 1.3–2.5) for all subjects (Table III). Table IV shows the odds ratio for a history of falls, physical activity, calcium intake, smoking and drinking when all these factors were used as independent variables in the same conditional logistic regression model. The odds ratio thus obtained for a history of falls was 1.8 (95% C.I. = 1.3–2.5) i.e. exactly the same as that obtained when a history of falls was used as the only independent variable. This indicated that the effect of

Table I The age and sex distribution of subjects with hip fracture

Age group	Male	Female
Younger than 70	47 (38.9%)	54 (19.2%)
70 to 79	45 (37.2%)	108 (38.4%)
80 and over	28 (24.0%)	118 (42.3%)
Total	120 (100%)	280 (100%)

Table II The reported activity when hip fracture occurred

Cause	Percentage
Falling while walking on the level	50
Falling while walking on slope	1
Falling while running	1
Falling from stairs or height	13
Standing up or sitting down	27
Traffic accident	2
Don't know	6
Total	100

Table III A history of falls in the preceding year and risk of hip fracture

Age group	Percentage of cases with positive history	Odds ratio (±95% CI)
Younger than 70	17%	4.3 (1.9–9.5)
70 to 79	20%	1.7 (1.0–3.0)
80 and over	23%	1.3 (0.8–2.2)
All	20%	1.8 (1.3–2.5)

Table IV Adjusted odds ratios (by conditional logistic regression with both controls matched to one case and using all variables in a model) for hip fracture

Factor	Odds ratio (±95% CI)
A history of falls in previous year	1.8 (1.3–2.5)
No falls	1.0 (–)
Physical activity	
Lowest level	1.7 (1.2–2.3)
Intermediate level	1.2 (0.9–1.6)
Highest level	1.0 (–)
Calcium intake	
Lowest quintile	1.9 (1.3–2.7)
Second quintile	1.7 (1.1–2.7)
Third quintile	1.2 (0.8–1.9)
Fourth quintile	1.2 (0.8–1.8)
Highest quintile	1.0 (–)
Current smoker	1.3 (0.9–1.7)
Non-smoker	1.0 (–)
Drinking every day	4.0 (2.3–7.0)
Not drinking every day	1.0 (–)

falls on hip fracture was not confounded by physical activity, calcium intake, smoking and drinking.

Among hip fracture patients with a history of falls, 16% were on anti-hypertensives, 0.25% were on sedatives, 1.75% had a history of stroke and 7% drank every day. These were not significantly different from the proportions in hip fracture patients without a history of falls (P larger than 0.05 by the t-test). 77% of patients with a history of falls and 81% of patients without a history of falls could go outdoors without any aid ($P>0.05$ by the t-test). Only 10% of all hip fracture patients walked outdoors daily.

Discussion

Hip fracture is a common and an important public health problem. For instance, about 247,000 hip fractures occurred among persons over the age of 45 in 1985 in the United States with a total cost of $7.3 billion in 1983.[4] In the past, the fracture was uncommon among Chinese in Singapore[5] and Hong Kong[6], but recent evidence indicated that the incidence was increasing rapidly to western rates[1-7]. The prevention of hip fracture is as important in Hong Kong and other developing Asian countries as in Western countries.

We found that about 50% of hip fracture resulted from falling while walking on the level. Though some authors argue that the fracture lead to the fall, a more conservative and probable interpretation is that the falling was a direct antecedent of hip fracture in many patients[8].

In this study, the hospital and community controls represented the sick and the relatively healthy elderly living in the community. A history of falls in the preceding year was a risk factor for hip fracture when comparisons were made with both hospital and community controls. As using patients' history of falls was subjected to certain recall bias, a history of fracture was also obtained. A history of fracture was also more frequent in cases than controls, though this may imply that hip fracture patients fell more often and/or were more osteoporotic.

An adequate calcium intake and load-bearing activity may be important in preventing hip fracture in our population.[3] However, osteoporosis alone cannot account entirely for the exponential increase in incidence of hip fracture with age, and proneness to falls in the elderly may be as important.[9,10] Indeed, we found that a history of falls was significant in subjects younger than 70. This could be explained by the fact that the frequency of fall rises exponentially with age,[9] and the difference in a history of falls was smaller in older age groups. It has been suggested by Evans[11] and by Cooper[12] that above 75 years of age the neuromuscular response which protects the skeleton against trauma may be more important, and this may also apply to our population.

The risk factors for falls in the elderly were recently reviewed by Peck.[13] It was suggested that extrinsic risk factors for falls included treatment by sedatives, anti-hypertensives and alcoholism. Nevertheless, by comparing hip fracture patients with and without a history of falls in the preceding year, cardiovascular accidents, treatment by sedatives, anti-hypertensives and use of alcohol were found to be unrelated to a history of falls.

Hence, there is relatively little known cause of falls in our population. Nevertheless, the potential of exercise programmes in the prevention of falls and fractures are large. It has been shown that lack of load-bearing exercise is an independent factor for hip fracture.[3] Regular load-bearing exercise such as walking may enhance the protective mechanisms for injury after a fall[8], and evidence from a recent randomized trial indicated that exercise increased hip bone mass in post-menopausal women[14]. Exercise may also prevent many of the aging changes in the human body.[15,16]

It is concluded that liability to falls may be an important risk factor for hip fracture especially in the relatively younger elderly population. Though no obvious risk factors for falls have been discerned, the potential of regular load-bearing exercise in the prevention of falls and hip fracture in the elderly should be fully explored.

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